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OBESITY: ÆTIOLOGY AND METABOLISM.[1]

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By obesity is meant an excessive accumulation of depôt fat in the storage areas of the body. What constitutes excess will depend upon the point of view. The physician is called upon to regard obesity in one or more of the following ways: as a disfigurement, as a disease, as a "sign".

The æsthetic criteria of obesity may be determined by individual taste or even by the dictates of fashion. There comes a point, however, at which the deposition of fat impairs functional activity and gives rise to symptoms, so that a person may be said to be too fat if the adiposity results in distress or discomfort of any kind, impairs the sense of well-being or diminishes the capacity to enjoy life. Ultimately, by embarrassing the heart and respiration or by diminishing the resistance to disease, it may be a menace to life itself. On the other hand, even when it does not itself produce any deleterious results, obesity may be a feature of various disorders, some of which may shorten life. Here the prognosis will depend upon the disease with which the obesity is associated.

Since obesity may either itself endanger life or be associated with diseases which shorten life, it becomes important to know in a general way the extent of the correlation between adiposity and the expectation of life. This information is provided by insurance tables,[(1)] which indicate that when a very large number of individuals taken at random is examined, the expectation of life is diminished

[1] Read at the annual meeting of the British Medical Association, September, 1935. This paper has been published in an abbreviated form in *The British Medical Journal*, November 16, 1935.

among those whose weight exceeds by a certain percentage the mean of those individuals of the same height, age and sex who have passed as first class lives.

Various formulæ for calculating the "ideal" body weight have been deduced from the examination of large numbers of healthy individuals.[55] They yield results which correspond fairly closely to those of the insurance tables as regards the range of variation met with in health. It may be doubted, however, whether it is justifiable to assume that the weight should increase with increasing age, as the insurance tables indicate. The formulæ may therefore be more reliable.

Examples of such formulæ are the following:

Wt (kg) = 0·408 × Ht (cm) + 0·693 × stem length (cm) + 70·213. (Greenwood.)[56]

Wt (kg) = Ht (cm) − 100. (Broca.)

Wt (pounds) = 110 pounds for 5 feet and 5·5 pounds for each additional inch (males).
100 pounds for 5 feet and 5·0 pounds for each additional inch (females).[57]

The first of these formulæ is probably the best; the second is obviously a very rough approximation and is probably applicable only over a very small range.

The range of normal variation is taken as 15% to 20% above or below the predicted weight.

Such tables and formulæ furnish a standard of normality rather than a criterion of disease. They provide an objective and quantitative definition of overweight. It can only be inferred from them that in the presence of a deviation above or below the normal there will be a certain probability that disease capable of shortening life will eventuate. The significance to be attached to a variation in body weight in any single individual, however, can be determined only after taking into consideration all the facts of the case. The grade of adiposity can be expressed by the ratio:

$$\frac{\text{Actual body weight}}{\text{Ideal body weight}}$$

Accordingly 1 to 1·1 = normal; 1·1 to 1·25 = slight adiposity; 1·25 to 1·5 = medium adiposity; over 1·5 = marked adiposity.

While the insurance tables and formulæ for "ideal" weight are based upon data obtained from the measurement of a large number of individuals taken at random, perhaps a more accurate measure of normality might be obtained by selecting groups of individuals according to body build.[48] If this were done, many individuals might appear to be less abnormal than they would be if referred to the ordinary standards. The "correct" weight for an individual should in some degree depend upon the physical type to which he belongs. If this were more widely realized, many people would avoid ill-health and privation resulting from ill-advised attempts to cause their bodily configuration to conform to some general standard, whether that standard happened to be the mean value derived from ideal weight formulæ and insurance tables, or whether it was prescribed by fashion. "Be your type" is a sound physiological maxim which transcends the demands of fashion.

Normal Fat Metabolism and the Sources of Fat.

The depôt fat of the body may be derived from all three proximate principles of food. Fat is first broken down in the intestine into fatty acids, which form soaps and glycerol, but in the process of absorption through the intestinal wall these are again synthesized into fat, having a composition approximating to that of body fat. Fat, however, is not the only or even the chief source of the fat of the tissues. It has been shown by feeding experiments that carbohydrate is readily convertible into fat, and since it furnishes about two-thirds of the energy of an ordinary mixed diet, it is probably the main source of body fat. The available evidence seems to point to fat being formed by condensation of three molecules of glucose into fatty acid, which then unites with glycerol to form fat. The rapid conversion of large quantities of carbohydrate into fat tends to raise the respiratory quotient, which may go above unity, since a hydrocarbon rich in oxygen is being converted into one poor in that element, with the giving off of carbon dioxide.

Protein may likewise be a source of body fat under certain conditions; but it is doubtful to what extent this process occurs normally. Fifty-six *per centum* of protein is convertible into carbohydrate in the completely diabetic animal, and it is probable that when fat formation from protein does occur, it is indirectly through the conversion of the glutogenic amino-acids into carbohydrate, which in turn is converted into fat. It may be that in the normal organism triose formed in the course of intermediary metabolism from three carbon atom glutogenic amino-acids does not readily condense directly to form the hexose glucose, but is either rapidly oxidized or converted into glycogen. In these circumstances protein would form glucose and fatty acid only indirectly through glycogen. A reciprocal relationship appears to exist between glycogen and fat deposition in the organism. In general those conditions which lead to a deposition of glycogen in the liver also lead to an increased deposition of fat in the fat depôts and a simultaneous diminution in liver fat. Conversely, those conditions which cause a fall in liver glycogen also tend to lead to the mobilization of fat in the fat depôts and an increase of liver fat.

The fat in the fat depôts consists of neutral fat having a high degree of saturation. Before depôt fat is mobilized it is probably broken down into fatty acid and glycerol, to be again resynthesized into neutral fat in the blood, but little is known of the mechanism of this process. The liver probably plays an important part in fat metabolism, but its exact rôle is uncertain. It has been supposed to be concerned with converting the mobilized fat into a form more readily oxidizable by the tissues, as by the introduction of double linkages into the fatty acid molecule or building up the fatty acid mole-

cules into complex phospholipides, such as lecithin. Some doubt has recently been thrown upon this interpretation by Drummond[22] and others,[12][35][40] but it still remains a working hypothesis.

ENERGY METABOLISM.

In accordance with the law of the conservation of energy, if more energy is taken into the body in the food than is consumed, the excess foodstuff must be stored. Since the capacity of the body to store protein and carbohydrate is limited, the excess of foodstuff is chiefly stored in the form of fat. Owing to the high fuel value of fat, energy can be stored in smaller bulk in this form than in any other. Conversely, if the consumption of energy by the body is greater than the amount supplied in the food, the body draws upon its stores of energy in order to make good the deficiency. The carbohydrate stores are the most readily available, but, having a limited capacity, they become rapidly depleted. The depôt fat is then drawn upon. Finally, the body protein tends to break down. In view of these facts it is reasonable to suppose that obesity would result whenever there was a long-continued excess of intake over output of energy. It is necessary, however, to examine this question more closely.

Energy Requirements.

The energy requirement of the body is the amount of energy necessary to cover the following: (*a*) the basal metabolism, (*b*) bodily activity, (*c*) the specific dynamic action of food.

Basal Metabolism.—The basal metabolism is the amount of energy consumed by the organism when at complete rest and in the post-absorptive condition, that is, at least fourteen hours after the last meal. It is proportional to the body surface and not to the body weight. For this reason body weight is not a reliable guide to the caloric requirement, especially when dealing with very thin and very obese persons. Doubling the weight, for example, would not double the body surface or the basal metabolism. An increase of weight does not add greatly to the caloric requirement, nor to the amount of food which should be taken, a point of practical importance. The standard figures for normal basal metabolism for an individual of a given age, sex, height and weight can be found either by referring to the Harris and Benedict[33] prediction tables or by employing the Du Bois[23] formula for estimating body surface, and the Du Bois table giving the calories per square metre of body surface per hour for age and sex. For example, using the Du Bois formulæ, a man 70 kilograms in weight, 170 centimetres in height, and 24 years of age, would have a body surface of 1·8 square metres and a basal metabolism of 1,706 calories per twenty-four hours. The observed basal metabolism is expressed as a percentage of the predicted figure, a normal range of variation of $\pm$ 10% being allowed.

Activity.—A rough approximation to the number of calories to be allowed for activity may be obtained by taking the average starvation metabolism for an individual engaged in a certain kind of activity and subtracting from this value the figure for basal metabolism. For example, the average starvation metabolism of a vigorous man at light work and weighing 70 kilograms is approximately 2,240 calories, or 32 calories per kilogram for twenty-four hours. Subtracting the figure for the basal metabolism (1,760 calories), the number of calories allowed for activity would be 534.

Specific Dynamic Action.—It has been shown that the proximate principles of food, besides yielding a definite number of calories per gramme undergoing combustion, have a stimulating effect on metabolism due to a drug-like action upon cellular activity exerted by certain chemical substances formed in the process of intermediary metabolism.[41] For example, protein, which exhibits this action in the highest degree, causes a rise in metabolism equivalent to 17% of the caloric value of the food. In the case of carbohydrate, the rise is 9%, and in the case of fat 2·5%. This stimulating action of food upon metabolism is known as the specific dynamic action and, of course, enough energy has to be supplied to cover the specific dynamic action of the food itself, as well as that necessary to meet the calories required for basal metabolism and activity. Taking an individual on an average mixed diet, the maintenance requirement according to Rubner is between 11·1% and 14·4% above the starvation minimum.[41] For an individual whose maintenance requirement is 2,240 calories, as in the above example, the number of calories to be allowed for the specific dynamic action of the food would be between 248 calories and 322 calories, with a mean value of 285 calories.

Summarizing the results for our examples, the total caloric requirements for an individual of 70 kilograms in weight, 170 centimetres in height, and 24 years of age, doing light work, would be distributed as follows:

Basal metabolism	1,706 calories
Activity	534 calories
Specific dynamic action	285 calories
Total	2,525 calories

Or approximately 36 calories per kilogram for twenty-four hours. This is the amount of energy which would have to be taken in the food in order to maintain such an individual in caloric equilibrium.

Energy Balance.

In view of the bearing of the energy balance upon the problem of obesity, it is necessary to inquire how the various factors concerned may vary under different conditions and what importance is to be attached to such variations.

If we try to strike an energy "balance sheet", we find that on the one side of the account there is the supply of energy, which is derived entirely from the food, and on the other side there are the factors concerned with the consumption and dissipation of energy.

Credit Side.

Food.—Under physiological conditions the intake of food in most animal species is regulated by the proper correlation between appetite and physiological need. In the human subject this correlation is apt to be upset for various reasons. The inducements to excessive consumption of food under the conditions of modern civilization are numerous. The abundant supply of food of all kinds and the preparation of foods in such a way as to render them appetizing, easily digested, of small bulk and low satiety value, and in such a form as to reduce mastication to a minimum, all conduce to excessive caloric intake. The social temptations to excessive eating and the consumption of alcohol are also of importance, especially in certain walks of life, and so gluttonous habits are not infrequently formed. The tendency to routine in human society leads to the persistence of eating habits once they have been acquired. Such habits may have been physiological at one period of life, but may cease to be so with altered conditions of activity, particularly with advancing years. Excessive consumption of food may be customary in certain families, the members of which receive *"Une éducation morbide"* at the overladen family table. Certain races are also prone to habitual over-eating.

It is not to be supposed, however, that the consumption of large quantities of food in obese persons is always to be attributed to such causes as the above. In some cases it should be regarded as a response to a physiological need. This applies especially to persons with a high carbohydrate tolerance in whom excessive hunger resulting from hypoglycæmia, especially before meals, often accompanied by a specific craving for carbohydrate, may lead to increased intake of food.

While all kinds of foodstuffs contribute their quota of calories, carbohydrate is of special importance. It is cheaper than either protein or fat, less unappetizing than the latter, and while it is more bulky in the form of starch, it can be given in concentrated form as saccharose or glucose, which have the additional property of sweetness that renders them tempting. Not only is carbohydrate the chief constituent of the normal diet, but mechanical work can be performed more efficiently upon it than upon either protein or fat, with a consequent saving of calories.[41] Alcohol is a food of fuel value only a little less than that of fat, and it is burned in preference to carbohydrate, protein or fat, thus sparing the last mentioned, but severe mechanical work cannot be performed as economically upon it as upon other foodstuffs, although the difference is less obvious on mild exertion only.

In order that food may be available as a source of energy, it must, of course, be absorbed from the alimentary canal. In the presence of defective digestion and absorption, large quantities of food may be taken without fat deposition, even in persons otherwise predisposed to obesity. On the other hand, there is no evidence that food is more completely absorbed in obese than in lean persons, although it has been suggested that this might be the case in individuals of the sthenic habitus who are supposed to have a relatively long small intestine.

Because food intake is the only item on one side of the energy balance sheet, and because it is capable of the greatest range of variation, it is by far the most important single factor capable of disturbing the energy balance. Many obese persons claim to be small eaters. This statement should always be accepted with caution and after careful inquiry into the full details of the diet. It is, however, an undoubted fact that many obese persons maintain their weight on diets well below the average and rapidly put on weight on diets which fail to cause increased fat deposition in other persons of similar age, sex, size and mode of life. Food consumption is therefore only one of the factors to be reckoned with in the causation of obesity.

Debit Side.

Basal Metabolism.—Coming to the debit side of the energy balance, it will be observed that the factor of the greatest magnitude is that of the basal metabolism. It might therefore be anticipated that changes in the basal metabolism would be of great significance and that a lowered basal metabolism would afford a ready explanation of obesity, particularly in persons who are moderate in their consumption of food. Actual observation, however, shows that while in a certain percentage of cases the basal metabolism is lowered, in the majority it is normal, while in a small number it is actually above the normal range.[6] The finding of even a normal basal metabolism in very obese individuals points to an actual increase in the metabolism of the active tissues, since a large portion of the mass of the body is made up of comparatively inert fatty tissue.

It appears, therefore, that the presence of obesity is compatible with lowered, normal or increased basal metabolism, while, conversely, a basal metabolic rate well below the normal may be encountered in persons who are not obese. Patients with diminished thyreoid activity, whether primary or secondary to changes in other glands (for example, the pituitary), form the bulk of those with lowered metabolism. The normal lowering of metabolism in the senile period, unless compensated for by diminished intake of food, may disturb the caloric balance.

It is therefore evident that changes in basal metabolism may cause a considerable disturbance in the energy balance, but only in a small proportion of cases is a lowering of basal metabolism to be regarded as a significant factor in the causation of obesity.

Various Factors Influencing Metabolic Rate at Rest.—1. Drugs and toxins. All those agents which tend to stimulate metabolism, even when the individual is at rest, will increase the consumption

of energy and therefore militate against the occurrence of a positive energy balance. Among these are drugs such as thyreoid extract and dinitrophenol, also the toxins of disease, endogenous and exogenous. The loss of weight in fevers and in the various toxæmias is familiar. Drugs which stimulate metabolism are used therapeutically in obesity and they are of value chiefly in those cases in which the metabolism is lowered. Drugs which depress metabolism have not been shown to be of importance in relation to obesity.

2. Emotions and temperament. The metabolic rate is also increased by emotion, especially worry, and in these circumstances weight may be lost. This is probably due to increased muscular tone and to a disturbance in the autonomic control of the liver and endocrine glands (especially the suprarenal), and to some extent the heart and viscera.

Since absence of emotion saves calories, it might be expected that phlegmatic persons would be more prone to obesity. Contrary to the popular impression, however, the majority of obese individuals consider themselves excitable rather than placid;[24] but this excitability may be cortical rather than vegetative in origin.

3. Temperature. Exposure to external cold leads reflexly to increased metabolism and heat production to compensate for the heat withdrawn from the body. Heat loss and compensatory heat production are also promoted by the movements of air, which carry away heat and moisture, and by diminished humidity, which leads to increased evaporation and consequent cooling. The converse series of changes occurs as a result of exposure to external warmth, increased humidity and diminished movements of air. Excessive heat and humidity, however, increase metabolism.

In view of these facts it might be supposed that a warm climate would be conducive to obesity, while the opposite would hold for a cold climate. The rôle of climate would probably be more important were it not for the wearing of clothing and the use of artificial heating, the effect of which is to prevent any great change in the immediate environment of the body, which is made to approximate to that of a subtropical climate.

There is no evidence that obesity is commoner in warm than in cold or very hot climates; nor is there any evidence that excessive clothing is commoner among obese persons. It is difficult, however, to assess the effects of climate upon fat deposition in the presence of such variable factors as differences in activity, diet and water balance, not to mention the effects of endemic disease. The question requires further investigation. That changes in external temperature are not without influence, in spite of clothing, is suggested by the fact that persons of fixed habits in regard to food and exercise tend to become lighter in winter than in summer.

Cold baths increase the metabolism considerably. Immersion for five minutes in a cold bath at 15·5° C. (60° F.) causes the loss of about 70 calories; but the calories lost in this way form but a small fraction of the total heat loss for the twenty-four hours.

The heat-regulating mechanism is disordered in obesity, there being diminished heat loss by radiation, compensated to some extent by increased loss by evaporation, as manifested by excessive sweating. These should be regarded as effects rather than causes of obesity, since they are primarily due to the fact that fat is a bad conductor of heat. Owing to the heat-regulating mechanism being thrown out of gear, fat persons are ill-adapted to performing mechanical work under hot conditions.

4. Circulatory and respiratory disorders. In affections of the circulatory and respiratory organs increased work performed by the muscles of respiration or by the heart itself may lead to a definite increase in energy consumption, sometimes amounting to about 50% of the normal basal metabolism. Considering the stress which has been laid upon basal metabolism in endocrine disorders, it is remarkable that so little attention should have been paid to the increase in metabolism in other conditions and its relation to obesity and leanness.

Exercise.

The energy supplied in the food may be consumed by its being converted into mechanical work. Compared with that required for basal metabolism, the amount of energy which is converted into mechanical work constitutes a relatively small proportion of the total energy consumed in the twenty-four hours. In the example quoted, for a man of 70 kilograms doing light work it was only a little over one-third of the basal metabolism. Only in individuals doing very heavy kinds of work does the energy required for work approximate that of the basal metabolism. This is only to be expected when the energy equivalent of heat and work is considered. According to Joule's equivalent of heat and work, one calorie is equivalent to 426·5 vertical kilogram-metres, that is to say, a relatively large amount of work corresponds to a small amount of heat. The water of Niagara Falls, for example, can be utilized for conversion into a large amount of mechanical work, but the temperature of the water at the foot of the falls when no mechanical work has been performed is raised by churning to only a fraction of a degree above that at the top.

The amount of mechanical work which would have to be performed by a man weighing 60 kilograms in climbing the Eiffel Tower, which is 300 metres, or a little less than 1,000 feet, high, is equivalent to 42·2 calories.

$$\frac{60 \text{ kg.} \times 300 \text{ (metres)}}{426{\cdot}5} = 42{\cdot}2$$

But since the mechanical efficiency of the body (that is, the ratio of mechanical work done to the total energy evolved) is only about 20%, this figure would have to be multiplied by 5, so that the total

amount of energy which would be consumed would be equivalent to 211 calories, or about the amount of energy which is contained in a glass of milk or two oranges.

Again, it is found experimentally that an individual walking at less than 80 metres per minute (three miles an hour) along the level uses 0·0005 calorie per horizontal kilogram-metre.[7] Therefore, a man weighing 70 kilograms, going for an hour's walk and covering two and a half miles, would require only 140 calories, or approximately the amount of energy contained in a slice of bread.[1] According to Dodds's[20] computation, a person playing a hard game like squash rackets for half an hour would use up only 300 calories, or the energy supplied by a pint of beer, or two slices of bread and butter, or a double whisky and soda, or two dry Martini cocktails.

There is no evidence that the mechanical efficiency of the body is greater in obesity than in normal persons. If it were, work could be carried out more economically and more energy would remain for storage. In cases of marked obesity the mechanical efficiency is actually decreased.

These facts indicate that in the treatment of obesity it is much easier to produce a negative caloric balance by reducing the food intake than by increasing the amount of exercise. Apart from this, there may be disadvantages in prescribing exercise during a reduction cure owing to its stimulating the appetite. Of course strenuous exercise is definitely contraindicated when circulatory embarrassment is present.

Leaving out of account the basal metabolism, which is usually normal in obesity, exercise comes next to food intake in the order of magnitude and variability among the factors capable of disturbing the energy balance. Restricted bodily activity therefore plays a definite, although subordinate, rôle among the influences tending to produce a positive energy balance.

Obesity is commoner among persons of sluggish habits and sedentary occupation. Many persons date their obesity from a period of enforced rest, as during an illness or pregnancy. The greater incidence of obesity in the female sex may also be partly attributable to these factors. On the other hand, a great many obese people are very active in their habits, and inactivity is often a late effect of obesity, leading to the production of a vicious circle.

Specific Dynamic Action.—The energy consumed as a result of the specific dynamic action of food constitutes a smaller fraction of the total energy involved than that represented by any of the factors hitherto considered. In order of importance it comes next to muscular activity. Normally its value varies with the kind and amount of food taken. When protein is the basis of the diet, the specific dynamic action is enhanced by exercise, there being a summation of effects, as shown by Rubner.[52] The evidence with regard to any alteration in the specific dynamic action in obesity is at present unsatisfactory, largely owing to technical difficulties as well as to the difficulties in interpretation. The available evidence seems to point to its being diminished in many cases.[53] A negative specific dynamic action after the administration of carbohydrate has been reported. In other cases no change in the specific dynamic action has been observed.

[1] 70 kilograms × 2·5 (miles) × 1,609 (metres in a mile) × 0·0005 (calorie per horizontal kilogram-metre) = 140·7.

Over-Nutrition and Luxus Consumption.

According to the principle enunciated by Pflüger, the energy consumption is determined not by the supply of energy, but by the demands of the tissues, any excess of intake over the requirements being immediately stored, chiefly as fat. If this were true, any continued, even slight, excess of intake over requirement would eventually result in obesity. Von Noorden[46] has computed that a daily excess intake of 200 calories, corresponding to the amount contained in 300 cubic centimetres (ten ounces) of milk, would lead in the course of a year to a deposition of 7·8 kilograms of fat, or, allowing for the water content of fat tissue, an increase in weight of 11 kilograms (24 pounds). Two hundred calories are represented by such a small amount of food that neither eyesight nor appetite would appreciate it. It is a matter of common observation, however, that there are people who are big eaters and who, in spite of leading a sedentary life, free from worry and with plenty of sleep, fail to increase in weight, while others of similar age, sex and height, who take only a fraction of the amount of food and lead a more active life, become fatter. The fact that individuals differ so greatly in these respects indicates that the problem of obesity is not just one of the adjustment of the energy balance in terms of the estimated requirements.

A failure to lose weight on diets much below the estimated requirements or even on a basal caloric intake without complete rest,[53] is usually to be explained by one or more of the following: water retention, lowered metabolism, or a lack of correspondence between the estimated and the actual energy requirements. Water retention may result from starvation, but in some cases of obesity it is so pronounced as to suggest some involvement of the neuro-hypophyseal mechanism regulating water metabolism—a condition which would be the reverse of *diabetes insipidus*. Lack of thyreoid secretion is also conducive to water retention. Failure to lose weight is not synonymous with failure to lose fat. In estimating the caloric requirement, it is necessary to bear in mind that starvation leads to a lowering of metabolism; but even when the basal metabolism has been experimentally determined, it cannot be assumed that the value obtained represents a minimum for the twenty-four hours, since the metabolic rate during the hours of sleep may be lower than the waking basal metabolic rate. The continuous determination of the actual number of calories consumed by an individual during the waking and the sleeping hours and over a sufficiently

long period (days or weeks) to make the necessary observations regarding body weight and water balance during a reduction cure would present formidable technical difficulties, but this is precisely the kind of investigation which would be necessary for the solution of some of the outstanding problems of obesity.

It goes without saying that if the energy intake is less than the energy consumption, there will be a loss of energy-yielding tissue, otherwise the laws of the conservation of energy and mass would be contravened. There is no question that in the presence of a negative energy balance every individual, obese or otherwise, will lose tissue substance, even although different individuals may present differences as regards the relative rates at which the various tissues disappear. This forms the rational basis of treatment in all forms of obesity. The fundamental problem in obesity is not so much what occurs when less food than that necessary to meet the energy requirements is ingested, but what happens to the food which is taken in excess of the caloric requirements. There are five possibilities. The body may deal with the excess by: (i) limitation of absorption, (ii) elimination, (iii) increased mechanical work, (iv) combustion (luxus consumption), (v) storage.

There is no evidence that the first two play any important rôle. The fæces may be increased in bulk after the ingestion of a large amount of food, but it remains to be shown whether they contain any significant increase in the amount of food which has escaped digestion. There is likewise no evidence that an intake of food above the requirements at the moment leads instinctively to a subsequent increase in bodily activity. Storage is, of course, a well established method; the question of luxus consumption requires further consideration.

It is a noteworthy fact that the body weight normally tends to remain remarkably constant in spite of wide fluctuations in food intake and bodily activity, so that the body would appear to have some means of automatically regulating its weight. One of the means by which the body adapts itself to under-nutrition is a lowering of the metabolism. It would not be surprising, therefore, if it responded to over-nutrition by an increase in metabolism. Rubner,[51] in an experiment upon the dog, showed that when the animal was fed on a large quantity of meat over a period of several days, not only was the usual specific dynamic action of protein observed, but there also occurred a continued "secondary" rise in total day-to-day metabolism which increased progressively so long as the over-feeding with protein was continued. It is evident, therefore, that in the dog a luxus consumption may occur. Grafe[30] and his co-workers have extended these observations. They have shown that in the dog a rise in specific dynamic action and a total rise in metabolism may occur with or without a concomitant rise in basal metabolism. It is unfortunate, however, for the solution of the problem in man that most of the recorded observations upon luxus consumption have been made upon carnivorous animals (dogs) fed almost entirely upon protein, upon animals or human beings who had previously been under-nourished, or on patients convalescent from disease. Few observations have been made upon healthy human beings, and these have not been entirely convincing. The demonstration and quantitative estimation of luxus consumption in man would require a complete and continuous determination of the energy and material exchange over a much more extended period than has hitherto been attempted.

Although conclusive proof of the existence of luxus consumption in man is not yet forthcoming, the available evidence points strongly in this direction. While we must be content for the present to regard luxus consumption in human beings as an hypothesis, it is of interest to inquire what bearing it would have upon the problem of obesity and whether it would throw light upon any of the phenomena which do not otherwise seem to have received a satisfactory explanation.

The first question it raises is that of the definition of over-feeding. From one point of view over-feeding is an excess of food intake over energy requirements. In this sense most people over-eat. But if over-feeding is to be regarded as an intake of food in excess of that which can be dealt with normally by the mechanism regulating the constancy of body weight, then fewer people might be said to over-eat. If luxus consumption is involved in this mechanism, it follows that its normal limits must be ascertained before a satisfactory definition of over-eating can be given, and this could be determined experimentally only after examining a large number of individuals. The difficulties would be formidable, but without this information it would also be impossible to define with precision and in quantitative terms what is to be understood by nutritional obesity, a condition which has reference to the effect of excessive food intake upon an otherwise normal subject. In the absence of experimental data, it is only possible to surmise from indirect evidence the amount of luxus consumption which might be expected to occur normally.

While the average intake of food per head of population is approximately 3,400 calories (Atwater), the average physiological requirement is only 2,500 to 3,000 calories, so that there is an excess of 400 to 900 calories per head of population, and yet only a small proportion of the population is made up of obese persons. The excess of calories is equivalent to about 26% to 60% of the average basal metabolism (1,500 calories).

Since luxus consumption, as observed in the dog, for example, varies with the food intake, increasing up to a certain point as the food intake is increased, it would constitute an important protection against obesity, and the differences exhibited by different individuals as regards the readiness with which they put on weight might be due to variations in luxus consumption. According to this view, those individuals whose capacity for luxus consumption was at or above the upper limit of the normal range of variation, would remain lean even on a very large food intake. At the other end of the scale would be

those whose capacity for luxus consumption was at or below the lower limit of normality and who would in consequence put on weight readily in the presence of any excess of food intake over the actual requirement and who would in consequence tend to become obese in the absence of strict dieting. Between these extremes would come all those whose capacity for luxus consumption was within normal limits and who would put on weight only if the food intake was excessive.

Variations in luxus consumption would also help to explain why some individuals fail to put on weight in spite of a low basal metabolism, since it might be supposed that in such cases the excess of available fuel could still be burned off provided that a sufficient capacity for luxus consumption remained. Similarly, ability to maintain or even to put on weight notwithstanding the existence of a raised basal metabolism[49] might be accounted for by a low luxus consumption, provided always that the energy intake remained above the minimum requirement. From such considerations as the above it would appear that the various factors discussed under the heading of energy requirements and energy balance ought to be viewed in their possible relation to luxus consumption. Variations in these factors, either singly or in combination, would be significant in regard to the genesis of obesity only in so far as they resulted in a load being thrown upon luxus consumption which was beyond the capacity of that mechanism to deal with adequately.

Intermediary Metabolism.

Endocrine and Nervous Control.

Assuming that luxus consumption occurs normally and that diminished luxus consumption is a cause of obesity, it would make no difference from the point of view of energy whether such a diminution in luxus consumption was brought about primarily by decreased burning of the excess food or by increased storage or by a combination of both factors.

Diminished Combustion.

Deficient combustion would seem to be a factor only in that small group of obesities associated with a lowered metabolic rate, and especially with diminished thyreoid activity. Eckstein and Grafe[25] have shown that luxus consumption no longer occurs in dogs after thyreoidectomy. The evidence regarding the effect of removal of the pituitary gland upon the specific dynamic action of food[45] is conflicting. On the other hand, it is claimed that no rise in metabolism occurs after administration of glycine (Foster and Smith[28]). Loss of the thyreotropic hormone might be expected to produce some change in the specific dynamic action. The effect of removal of the pituitary upon the "secondary" rise in day-to-day metabolism has not been studied. Removal of the gonads is said not to reduce luxus consumption,[30] but no more does it produce obesity in most animals. In the human subject the tendency to obesity after ablation of the gonads increases with increasing years, but this may be due to a failure of compensatory changes in the thyreoid and pituitary glands. Administration of excess of certain pituitary hormones (? gonadotropic) over a prolonged period also results in a lowering of metabolism, diminished thyreoid activity and obesity (Thompson and Cushing[17]). In the great majority of cases of obesity, however, there is reason to believe that the metabolism of the active tissues is if anything increased, and it is improbable that in these cases the defect underlying the obesity is to be attributed to diminished combustion.

There is no evidence that the obese exhibit any specific inability to burn fat, whether the fat is administered or derived from the fat depôts during starvation (*vide sequente*); nor is there any evidence that the liver, which is supposed to be concerned with converting fat into a form suitable for oxidation, is at fault. There is likewise, in the majority of cases, no evidence of any specific inability to burn carbohydrate. This is shown by studies upon the respiratory metabolism after ingestion of glucose,[29] and by the observation that there is no greater tendency to ketosis during starvation in the obese than in the normal individual, in spite of the fact that fat can be efficiently mobilized. Since the complete combustion of fat requires the simultaneous combustion of a certain amount of carbohydrate, the efficient burning of fat in these circumstances is indirect evidence of the efficient burning of carbohydrate. The ready conversion of fat into carbohydrate in the obese during starvation, which is suggested by the very low respiratory quotients observed under these conditions (*vide sequente*), may be partly accountable for the slightness of the tendency to ketosis.

Since the burning process does not seem to be at fault as a rule, there remains the second alternative, increased storage.

Increased Storage.

Increased storage might conceivably be due to some abnormality referable to the fatty tissues themselves: an anomaly of the mechanism of fat deposition, conservation and mobilization. On the other hand, it might be caused by some disorder of intermediary metabolism leading to increased formation of fat from other foodstuffs, especially carbohydrate.

Fat Deposition and Mobilization.—Increased fat deposition might result from an increased avidity on the part of the fatty tissues for circulating fat, but there is no proof of any specific anomaly of this character. Something of the kind may perhaps occur when a normal diet is resumed after a reducing cure in persons the bulk of whose fat depôts had previously been large. The rapidity with which fat is put on under these conditions depends to some extent upon the previous bulk of the adipose tissue.

An inability to break down and mobilize stored fat would result in a progressive heaping up of fat in the depôts. This occurs in lipomata and in conditions known as lipomatosis, but it is not observed in obesity. Metabolic studies upon under-nutrition

in obese persons indicate that the stored fat is mobile and very easily shifted into the metabolizing mixture (Keeton and Dickson[39]). This is shown by the fact that it is even more difficult to produce a negative nitrogen balance in the obese than in normal persons, the ample store of fat in the tissues being readily available to exert its "protein-sparing action".

Conversion of Carbohydrate and Protein into Fat.—Since it is from its glutogenic amino-acids that protein forms fat, the conversion of carbohydrate and protein into fat may, in the present connexion, be considered as one problem. If it could be shown that the essential peculiarity of metabolism in obesity consisted in an excessive conversion of carbohydrate into fat, a relatively simple explanation of many of the facts about the disease would be forthcoming. According to this theory, an excessively large proportion of the carbohydrate remaining after the energy requirements had been met would be converted into fat instead of being got rid of by burning (luxus consumption). This would be in keeping with the well known fact that in persons with a tendency to obesity the consumption of carbohydrate food in more than very moderate quantities readily leads to an increase in weight. It is difficult, however, to obtain decisive experimental evidence for or against this hypothesis. There is no evidence that the ingestion of carbohydrate causes a more rapid or pronounced rise in the respiratory quotient, towards or above unity, in obese than in normal persons.[29] But short experiments after massive doses of carbohydrate shed little light on the problem, since the respiratory quotient rises to or above unity even in normal persons under these conditions. In more prolonged experiments, without massive doses of carbohydrate which reproduce more natural conditions, the changes in the respiratory quotient are not sufficiently large to be significant. A low respiratory quotient and a smaller rise than normal after ingestion of glucose have been reported.[36] This might mean that carbohydrate was so much more rapidly converted into glycogen in the early stages of the experiment than in the normal that less was available for conversion into fat. The very low respiratory quotients found in fasting or in undernourished obese subjects have suggested to Lyon, Dunlop and Stewart[43] that under these conditions fat was being converted into carbohydrate. This might indicate that the reaction carbohydrate $\rightleftarrows$ fat is readily reversible in the obese, the direction of the change depending upon the food intake and the state of nutrition. Since, however, the respiratory quotient represents only a "dynamic equilibrium" in which many different kinds of reaction having opposing effects upon the quotient[11] are concerned, it is open to so many interpretations that it cannot be regarded as a reliable guide to what is occurring.

Lyon[42] has shown that when obese persons are put on a reducing diet yielding a constant number of calories, but containing different amounts of carbohydrate, protein and fat, and the rate of loss of weight is compared after withdrawal of one or other of these foodstuffs and its replacement by an isodynamic quantity of the remainder, the most rapid reduction occurs when carbohydrate is diminished; next comes protein, while in the case of fat the amount does not make any difference. The converse also holds. Upon a constant caloric intake fat appears to be the least liable to cause an increase in weight if added to the diet, and the least liable to cause loss of weight if withdrawn from the diet, while the reverse holds for carbohydrate. These results show in a striking fashion the importance, so far as the treatment and genesis of obesity are concerned, of the kind of foodstuffs taken. It has not been demonstrated, however, whether the character of the response in obese persons differs from that of normal individuals subjected to similar variations in diet.

Hagedorn, Holten and Johansen,[32] as a result of a comparison between normal and obese persons with regard to diet, exercise, rest, respiratory quotient and weight, have concluded that in obesity there is an abnormal formation of fat from carbohydrate.

The plasma cholesterol is usually within normal limits in obesity,[8][38] but it may be increased when hypothyreoidism is present and in those obesities which are associated with degenerative diseases of the vessels, glycosuria, arthritic changes *et cetera*. It may also be elevated as a result of starvation during a reducing cure. In the present state of our knowledge regarding lipoid metabolism, it is difficult to know what interpretation is to be placed upon these findings.

The importance of the interrelationship between carbohydrate and fat metabolism in obesity is further brought out when the rôle of the endocrine glands and nervous system is considered. Although there are still important gaps in our knowledge, the evidence, so far as it takes us, seems to indicate that lesions or functional disturbances of the endocrine glands and nervous system of a kind leading to obesity, lead also to the deposition of glycogen in the liver. In this respect the endocrine obesities would come into line with obesities due to over-feeding. For example, the administration of insulin together with carbohydrate causes glycogen to be laid down in the liver, and this has been used as a means of fattening people. The islets of Langerhans have been reported by Ogilvie[47] to be hypertrophied in obesity, but it is not certain whether this is to be regarded as a primary or as a compensatory phenomenon.

While thyroxin causes the mobilization of liver glycogen, deficiency of thyreoid secretion has the opposite effect and, corresponding with this, obesity is a not infrequent accompaniment of hypothyreoidism.

Basophile adenomata of the pituitary gland give rise to marked obesity. The more important features of pituitary basophilism, including obesity (but not hypertension), have been reproduced experimentally in the dog by the injection of anterior pituitary extracts (Thompson and Cushing[17]), and one of

the most striking results of this administration was the deposition of an enormous amount of glycogen in the liver cells, comparable with that which is found in von Gierke's disease. Although the extracts employed were stated to be rich in gonadotropic hormones, it is not certain whether the action is to be attributed to these or to the presence in the extracts of other hormones, and especially of a distinct hormone having a stimulating action upon the suprarenal cortex (adrenotropic). The fact that a similar, if not identical, syndrome occurs in the presence of tumours of the adrenal cortex and of the thymus suggests that the obesity associated with tumours of these glands may be brought about by a similar mechanism and would presumably be accompanied by similar changes in liver glycogen. In this connexion it may be mentioned that while double adrenalectomy in cats causes the glycogen reserves of the liver to be depleted, this effect is corrected by the administration of cortical hormone along with glucose, but not by glucose alone.

Partial destruction of the anterior lobe of the pituitary gland in young animals (puppies) may result in obesity,[15] and small tumours (for example, craniopharyngiomata, chromophobe adenomata) confined to the *sella turcica* without any possibility of their pressing upon the *tuber cinereum*, give rise to adiposity and an increased sugar tolerance. The obesity resulting from such lesions, unlike that of pituitary basophilism, is probably to be attributed to deficient secretion, although it is sometimes difficult to be sure whether such lesions act by irritation or by suppression of function. If this interpretation be correct, then the increased sugar tolerance would point to there being a lack of hormones having the reverse action with respect to carbohydrate tolerance. The diabetogenic and thyreotropic hormones would come into this category. Since these hormones produce effects which correspond to those of diminished insulin action and increased thyreoid secretion, a lack of them might be expected to produce effects resembling those of increased insulin and diminished thyreoid secretion, and amongst those would be the deposition of glycogen in the liver. Unfortunately no data seem to be available regarding the glycogen content of the liver in animals suffering from obesity due to partial destruction of the anterior lobe of the hypophysis.

Little is known regarding the obesity which sometimes follows ablation of the gonads, but it is possible that it may be due to secondary changes occurring in other endocrine glands, especially the thyreoid and pituitary. It has recently been shown that removal of the ovaries in the rat increases the glycogen content of the liver (Gullick, Samuels and Denel[31]), but further studies are desirable regarding the relationship between liver glycogen and the functional activity of the gonads.[10][5]

Experimental lesions, tumours and inflammatory disease (for example, encephalitis) of the hypothalamus sometimes result in obesity. Foster and Benninghoven[27] have presented data suggesting that in animals suffering from obesity due to experimental lesions of the hypophysis there is an increase in liver glycogen, but the number of animals in their experimental series was inadequate. The liver fat in these animals was also increased, thus providing an exception to Rosenfeld's generalization that when the liver fat is high the glycogen content is low and *vice versa*. In order to understand how this result could be brought about it would be necessary to know how the hypothalamus controls carbohydrate and fat metabolism. It has long been known[44] that stimulation of the sympathetic (adrenergic nerves) causes increased adrenaline secretion and glycogenolysis, while the parasympathetic (cholinergic nerves) has the opposite effect. Clark[13] has brought forward evidence which indicates that stimulation of fibres (presumably cholinergic) in the right vagus causes the islets of Langerhans to secrete insulin. A considerable body of evidence (recently summarized by Cushing[16] and by Beattie[2][3]) has now accumulated to show that the hypothalamus has physiological and anatomical connexions with the autonomic nervous system, the anterior hypothalamus being concerned with the production of parasympathetic effects and the posterior hypothalamus with sympathetic phenomena. Further, the posterior hypothalamus is evidently under the control of the anterior hypothalamus, while both receive fibres from the thalamus. In view of the existence of such mechanisms, it would be easy to understand how lesions or functional disorders in the hypothalamus could influence carbohydrate metabolism through the autonomic nervous system. When the disorder was such as to give rise to a predominance of anabolic (parasympathetic) over catabolic (sympathetic) functions, glycogen storage (and obesity?) might result. The question of the existence and location of definite "centres" controlling glycogen synthesis and glycogenolysis is, however, still debatable. The hypothalamus might also influence carbohydrate and fat metabolism through its nerve supply to the pituitary (diencephalo-infundibular fibres to the posterior lobe and sympathetic fibres to the anterior lobe) and possibly to other endocrine glands. The functional activity of certain of the metabolic centres in the hypothalamus is in turn influenced by pituitary secretion reaching them either through the infundibular canal or through the hypophysio-hypothalamic portal system. It is evident, therefore, that in discussing the relationship between dysfunction of either the pituitary or the hypothalamus and obesity, the neuro-hypophyseal mechanism has to be viewed as a whole. It is, of course, conceivable that excessive glycogen formation and obesity might result from interference with autonomic innervation due to lesions along the paths between the hypothalamus and the liver.[4]

The processes of glycogen synthesis and the conversion of carbohydrate into fat seem to be linked together in some way, but the exact nature of the underlying mechanism responsible for this interconnexion is unknown. The mere accumulation of glycogen in the liver is not, however, invariably

associated with obesity, for if the glycogen is excessively resistant to mobilization, as in von Gierke's disease, the tissues may be starved. The site of the conversion of glucose into fat is uncertain. Most probably it is the liver. If so, the resulting fat does not tend to accumulate in that organ, since the fat content of the liver is usually, although not invariably, diminished. It would appear, therefore, to be rapidly passed into the blood stream and conveyed to the fat depôts.

Examination of the sugar tolerance has been employed as a means of investigating the metabolism in obesity. The carbohydrate tolerance in obesity may be normal, increased or diminished. An increased sugar tolerance might result from increased functional activity of the islet tissue of the pancreas or from diminished secretion of hormones which antagonize insulin, such as thyroxin and certain pituitary hormones, particularly the diabetogenic hormone; or again, it might be due to certain lesions of the hypothalamus in situations similar to those which have been shown experimentally by Davis[19] to be capable of suppressing the hyperglycæmia and glycosuria following pancreatectomy, an effect resembling that which Houssay[37] found to follow removal of the hypophysis. In this connexion the importance of quantitative relationships is to be noted. The administration of excessive quantities of insulin, sufficient to produce hypoglycæmia, or the administration of insulin without an adequate supply of carbohydrate leads to a disappearance of glycogen from the liver and a loss in weight. This may be one reason why hyperinsulinism associated with pancreatic adenomata is not accompanied by obesity. Similarly, the emaciation which is found in complete, as contrasted with partial, destructive lesions of the pituitary, as in Simmond's disease (hypophyseal cachexia), may in part be due to chronic hypoglycæmia resulting from lack of the diabetogenic and possibly other hormones (? adrenotropic, ? thyreotropic, ? gonadotropic). In keeping with this is the finding that after complete experimental removal of the anterior lobe of the pituitary the liver glycogen is not increased and that which remains appears to be very resistant to mobilization (Corkhill, Marks and White[14]). A similar increase in the resistance of liver glycogen to mobilization, together with increased susceptibility to insulin, has been observed after complete thyreoidectomy in rabbits. This may be one reason why some cases of myxœdema are not associated with obesity.

Some forms of obesity, on the other hand, are associated with a diminished carbohydrate tolerance, often resulting in glycosuria. It is customary to interpret the diminished sugar tolerance as an exhaustion phenomenon due to prolonged overtaxing of the islets of Langerhans and/or to regard the obesity and glycosuria as the result of a common cause, namely, over-eating. While this may be the sequence of cause and effect in certain instances, there are many reasons for doubting the validity of this interpretation in all cases. For example, it would be difficult to understand why obesity should persist or even increase in spite of functional failure of the islets of Langerhans sufficient to result in marked glycosuria. Again, in the light of the recent work on the effects of high carbohydrate diets in diabetes, the exhaustion hypothesis has to be reconsidered. Most important of all, the experimental results obtained by Thompson and Cushing[17] in their work upon experimental pituitary basophilism provide an example of glycogen deposition, obesity and diminished carbohydrate tolerance produced in a comparatively short space of time as a result of the administration of pituitary hormones. It is evident that the diminished carbohydrate tolerance in this experiment must be brought about by some mechanism other than that which is at work in glycosuria resulting from loss of islet function, since glycogen was laid down in large quantities—the reverse of that which holds in diabetes following removal of the pancreas. This accords with the observation that ketosis is often remarkably slight in spite of the elimination of much sugar in the urine in glycosuria associated with obesity in the human subject. Evidence is therefore gradually accumulating which points to some forms of glycosuria, particularly those associated with obesity, being due to causes outside the pancreas and possibly referable to functional disturbances of endocrine activity similar to those which occur in pituitary basophilism. It would not, however, be justifiable to refer all cases of glycosuria associated with obesity to extrapancreatic causes, since pancreatic diabetes may occur in an individual predisposed to obesity from other causes.

CARBOHYDRATE TOLERANCE, HORMONES AND OBESITY.

A. Increased carbohydrate tolerance.

Pancreas:	Insulin (+ carbohydrate)	Syndrome of excess.
Pituitary:	Diabetogenic hormone	Syndromes of deficiency.
	Adrenotropic hormone (?)	
	Gonadotropic hormone (?)	
	Thyreotropic hormone	
Thyreoid:	Thyroxin	
Gonads:	?	

B. Diminished carbohydrate tolerance.

Pituitary (basophilism):	Adrenotropic or gonadotropic hormone?	Syndromes of excess.
Adrenals (tumours):	?	
Thymus (tumours):	?	

The available evidence therefore suggests that the essential change in intermediary metabolism underlying a large group of obesities is to be traced to a disturbance of hepatic function whereby glycogen is laid down and carbohydrate is converted into fat with excessive ease. This may be brought about by disturbances in the control of hepatic function due to change in the functional activity of one of the endocrine glands (with or without concomitant or compensatory changes in other glands or even in the same gland), or it may be due to changes in the central nervous system. In a very large proportion of cases of obesity there is an absence of collateral evidence pointing definitely to disease of this or

that endocrine gland or to focal disease of the nervous system. It might therefore be supposed that in such cases the disorder was one of the neuro-endocrine system as a whole, whereby the automatic control of the constancy of body weight became thrown out of gear. It would be difficult, however, to conceive of a specific anomaly of metabolism affecting all parts of such a complicated mechanism simultaneously, in the absence of some central coordinating mechanism. Such a mechanism may perhaps be found in the metabolic centres in the hypothalamic region of the brain, or perhaps more correctly in the neuro-hypophyseal mechanism considered as a functional unit. A functional derangement of this mechanism might be at the root of many cases of obesity—perhaps the majority. Obesity of this variety would be classified as neuro-endocrine. In view of the numerous functions which have been attributed to the hypothalamus and to the pituitary gland, and the evidence that both these structures may control the function of other endocrine glands, it ought not to be a matter for surprise that the endocrine picture in obesity should present so few constant features and that so many apparently "larval" forms of endocrine disturbance should be met with.

Of course the liver itself might be the seat of an anomaly of the intrahepatic factors (enzymes) concerned with glycogen formation and the conversion of carbohydrate into fat; but it seems unnecessary to invoke this hypothesis until it can be shown that the operation of the better known extrinsic mechanism controlling liver function is inadequate to explain the phenomena.

Distribution of Fat.

In view of the frequent difficulty of obtaining collateral evidence of focal disease or functional derangement either of endocrine glands or of the hypothalamus, it becomes important to inquire whether the origin of an obesity can be diagnosed from the distribution of fat. Most observers seem to claim that this is possible, and an apparently formidable array of evidence has been brought forward supporting this contention.[26]

I would, however, plead for a more critical attitude towards this question. If we confine our attention to the adipose tissue alone and leave out of consideration all such concomitant phenomena which affect the configuration and appearance of the patient, such as changes in the skeleton, the ligaments, the skin and its appendages, the subcutaneous tissues (for example, deposits of muco-protein in myxœdema), the muscles (atrophy of calf and thigh muscles in pituitary basophilism), the genitalia *et cetera*, is it quite certain that the fat can be recognized to have a characteristic distribution according to the cause of the obesity? If this is not certain, then in the absence of these concomitant changes the configuration of the patient would not provide any reliable clue to the specific origin of the obesity. Recent work, for example, indicates that after treatment of myxœdema with dinitro-o-cresol, the characteristic swellings due to deposit of muco-protein remain even when the fat is reduced.[21][9] It would perhaps be going too far to assert that the various endocrine glands have no specific control over the distribution of fat and that they influence only the amount that is deposited; we have only to think of the peculiar increase of fat in the orbit in exophthalmic goitre. The question requires experimental investigation. On the other hand, the physiological variations in the distribution of fat appear to be of so similar a character to those met with in disease that the possibility cannot be overlooked that the fatty tissues themselves, the inherited pattern of the fat depôts, may to a large extent determine the distribution of fat in obesity from any cause. It is not surprising, therefore, to find that even in obesities of known endocrine origin differences may occur in the distribution of fat in affections of the same gland, while the distribution of fat may be very similar in disease of different glands. According to this view it would not be possible to employ the distribution of fat as the criterion of the involvement of a particular endocrine gland in the absence of collateral evidence unless it were assumed that the normal variations in fat distribution are themselves determined by the relative preponderance of this or that endocrine gland, which would be a mere begging of the question.

The rôle of the fatty tissues is probably of primary importance in another variety of obesity which deserves further study. There are some stout persons who live an active life, eat in moderation and maintain a fairly constant body weight, but who exhibit no great tendency to put on weight on a liberal diet, and in whom no disorder of metabolism (sugar tolerance, basal metabolism, specific dynamic action, definite manifestations of endocrine disease *et cetera*) is detectable. In these the obesity appears to be structural and developmental (architectonic) rather than metabolic in origin. One has only to think of the differences in the development of fat in different varieties of the same species of animal (for example, dogs) to appreciate the probable nature of variations of this character. They probably represent extreme examples of a physical type. There seems no reason why the mass and distribution of the fatty tissues should not be determined by heredity, in much the same way as the size and structure of bones or the mass of muscles is so determined, granted, of course, modification by other factors.

Ætiology.

Obesity may be classified as developmental, metabolic or nutritional, and it may be hereditary or acquired.

A. Developmental.	Hereditary.
B. Metabolic:	
Endocrine.	Hereditary or acquired.
Neurogenic.	
Neuro-endocrine.	
C. Nutritional.	Acquired.

The developmental group would be wholly hereditary, the nutritional group wholly acquired,

while the metabolic group might be either hereditary or due to acquired disease of the nervous system or of the endocrine glands. In all varieties such variables as food intake and exercise play a part, although in the nutritional group they are the primary factors.

The influence of heredity is suggested by the fact that some 70% of the obese have overweight parents.[24] Daneforth,[18] in a study of hereditary obesity in mice, found that the condition was associated with a single dominant gene which acts as lethal when homozygous. In the case of the human subject, sufficient data are not yet available for genetic analysis.

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SOME ANATOMICAL CONSIDERATIONS OF THE AUTONOMIC NERVOUS SYSTEM.[1]

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THESE notes were prompted by reading Professor Wilkinson's paper upon the autonomic nervous system in THE MEDICAL JOURNAL OF AUSTRALIA of June 29, 1935. A summary is rarely completely satisfying to all; Professor Wilkinson has obviously succeeded very well both in compression and elimination. I would therefore join issue with him only in regard to a few features of his paper; there must necessarily be several minor points, which are either slips or matters of personal interpretation, and can be neglected. Passing by the

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physiological aspects, which Dr. Gilbert Phillips will discuss, there are four main points in his lecture that I would specially draw attention to. It is the custom to talk of definite centres in the hind brain (for example, vaso-constrictor, vaso-dilator, cardio-accelerator *et cetera*), and I see that in replying to Dr. Beare at the end of his lecture, Professor Wilkinson said that these were definite anatomical entities in the vagus nucleus. I have frequently considered this question, and so far as I can determine, there has been a lamentable lack of correlation between the experimental physiologist and the neurologist in this matter, and there is no definite certainty as to which of the numerous cell groups in the vagal group of nuclei are concerned with different functions, or even whether the real cell groups involved are not reticular ones underlying the vagal nuclei. It is even disputable whether exact and precise centres really do exist.

The next point to which I would draw attention is the diencephalon. Much confusion is given to the subject by the multiplicity of nomenclatures employed by various authors, and I think that the hypothalamic autonomic centres can be more clearly visualized if we name them according to their position: (*a*) in the *tuber cinereum* and *corpus mammillare*, (*b*) in the lower wall of the third ventricle (periventricular group), (*c*) in relation to the optic chiasma and tracts (supraoptic group). This topographical subdivision also enables us to appreciate more easily the suggestion of Beattie and others that there are two groups: an anterior (especially supraoptic) group concerned with parasympathetic functions, and a posterior group, probably concerned with sympathetic functions. The evidence that these hypothalamic centres receive afferent impulses from taste or from the viscera is at present almost wholly deductive, and we have practically no direct evidence of afferent fibres other than those of smell to these centres. In conclusion, I might perhaps say that a really satisfactory understanding of the hypothalamus requires a consideration of its probable evolutionary history from the fishes to man.

Thirdly, as regards the vexed question of the parasympathetic innervation of the colon, I think there is little doubt that the recent work of Telford and Stopford[1] has at last shown us the pathway from the sacral nerves upwards across the brim of the pelvis to the inferior mesenteric artery and thence to the distal part, if not all, of the colon.

On morphological grounds it would seem very unlikely that the vagus influence extends beyond the small intestine, and I can find no positive evidence to support the usual text-book statement that in man it supplies the colon as far as the transverse colon. Finally, in regard to the innervation of the heart, I feel that while Professor Wilkinson has made a most useful summary, both he and many others have failed to state fully the position, namely that besides the vagal supply to the smaller blood vessels and the sympathetic supply both to the heart muscle and larger coronary vessels, we also have a rich innervation of the sino-auricular nodes and Purkinje conducting fibres and the auriculo-ventricular bundle, and this innervation, whether vagal or sympathetic, must clearly be taken into account in considering the autonomic innervation of the heart. In this connexion, also, I feel that the one outstanding example of afferent nerve fibres in the autonomic nervous system, namely the carotid sinus branch of the ninth cranial nerve, surely should be mentioned, because of its fundamental importance in the regulation of blood pressure and respiration.[2] Finally, as I have already said in a letter to Professor Wilkinson, these criticisms are not written in any carping spirit, but solely in an endeavour to round off and make more complete in our own minds Professor Wilkinson's admirable summary.

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SOME PHYSIOLOGICAL CONSIDERATIONS OF THE AUTONOMIC NERVOUS SYSTEM.[1]

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HAVING read Professor Herbert Wilkinson's paper[1] entitled "The Autonomic Nervous System", delivered at a meeting of the South Australian Branch of the British Medical Association on March 28, 1935, I am moved to admire the competency with which he presented a detailed schema of a difficult subject to an audience whose interest in it would certainly be general rather than particular. It is with considerable diffidence, then, and only with the object of reconciling Professor Wilkinson's address with current neurological opinion, that I submit the following suggestions for the amendment of his interesting article.

In the first place may I quote the statement (page 802):

> . . . when impulses are discharged from the central organ through the somatic efferents, impulses are at the same time discharged through the autonomic efferent conductors. There can be no action in the somatic system without coincident action in the autonomic system.

In 1932 Adrian, Bronk and the present writer,[2] working at Cambridge, observed that the peripheral sympathetic nervous system, unlike the peripheral somatic nervous system, was the seat of persistent nervous discharges, pressor in function, initiated with a respiratory or occasionally a cardiac rhythm, and incapable of being modified by any peripheral nervous impulses (somatic) other than those which modified the central excitatory state of either the respiratory or cardiac centre. In spite, then, of this fundamental difference in the activity of the two systems (graded intermittent somatic and fixed immutable persistent autonomic discharges), the discharge in the cervical sympathetic trunk was precisely synchronous with that in the phrenic nerve, and both were controlled from the same central efferent mechanism, namely the respiratory centre.

We were not able to discover any somatic discharge at spinal levels to correspond with persistent discharge

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either in splanchnic nerves, mesenteric nerves or *rami communicantes*. Again in Figure I (page 803), in the diagram representing the innervation of skeletal muscle, the descending fibres, presumably cortico-spinal, are shown sending collaterals to "sympathetic centre in spinal cord", presumably intermedio-lateral horn cells, and this connexion is, I assume, represented as the neurological basis of Professor Wilkinson's hypothesis of "coincident action" in somatic and sympathetic conductors. There does not appear to be any certain evidence, histological or experimental, of the existence of such collaterals. Hoff,[3] working at Yale on the site of termination of the cortico-spinal pathways, has shown that all the pyramidal fibres end, not in relation with anterior horn cells at all, but around cells at the base of the posterior horn of grey matter, the implication being that internuncial neurones transmit impulses from here to the anterior horn cells. He does not describe any synapses of pyramidal fibres in the intermedio-lateral column. Fulton's[4] work, in which he describes changes in vascular and sweat reactions following lesions of the premotor cortex, suggests that possibly fibres from this region may terminate at spinal "sympathetic" neurones, although Walshe[5] has recently questioned his observations. However this may be, it is quite certain that fibres arising in the premotor cortex which do descend in the spinal cord in company with cortico-spinal fibres[6] are not responsible for the initiation of nerve impulses in peripheral somatic efferent conductors. It is perhaps unnecessary to labour this point when several examples of somatic activity unaccompanied by autonomic activity may be so readily recalled; but one may certainly ask: "Is there any evidence that an afferent fibre from a blood vessel (seen in Figure I) is able to influence anterior horn cells directly?"

To refer now to the statement, made on page 810, that "all efferent fibres which leave the central nervous system, namely somatic motor and autonomic preganglionic fibres, are said to liberate at their endings a substance akin to acetylcholine; and so these fibres are referred to as cholonergic".

Dale,[7] in May, 1934, published an excellent summary account of the transmission of the effects of nerve impulses, in which he speculates on the possibility of their chemical transmission by acetylcholine at somatic motor endings in the same manner in which it is now known that impulses are transmitted through sympathetic ganglia[8] and at parasympathetic terminations. He cites Adrian's conjecture[9] concerning transmission from motor nerve to voluntary muscle: "an excitatory substance liberated at a nerve ending, but destroyed within a few thousandths of a second . . . would account well enough for the known properties of a nerve ending".

Referring later to the same question, Dale remarks: "The observations are too new and too incomplete for detailed analysis of their meaning . . . but the apparent function of acetylcholine in transmitting the effects of impulses to nerve cells encourages one to expect a more general function for it in the transmission of motor nerve impulses to voluntary muscle".

It is quite likely that it will ultimately be found that acetylcholine or some other chemical substance is responsible for the transmission of motor impulses from somatic nerves to voluntary muscle; but on the present slender and more or less speculative evidence there seems to be no justification for regarding motor nerve endings as "cholinergic". Professor Wilkinson speaks also of the possibility that "further chemical research will demonstrate that the parasympathetic fibres also liberate a chemical substance antagonistic in action to that of sympathin which is liberated from the sympathetic endings". That this is already proven may be learnt by reference to the work of Englehart[10] in 1931 on the transmission of effects in the oculo-motor nerve, and that of Bacq,[11] who, in 1933, demonstrated that "sympathin" was liberated in the aqueous humour of the eye when the cervical sympathetic trunk was stimulated. This evidence is supported by the work of those authors quoted by Dale (*loco citato*), on the transmission of the effects of impulses in the *chorda tympani* and the work of Feldburg and others[12] on the liberation of adrenaline and acetylcholine in the suprarenal medulla during splanchnic stimulation. Further, in regard to the axone reflex (see Wilkinson's Figure XV), care must now be exercised, as a result of Matthews's and Barron's findings[13] that about 30% of all posterior root fibres normally carry impulses in a centrifugal direction before the participation of a central mechanism in this reflex is denied.

Reference should be made here also to the following statement, made on page 810 of Professor Wilkinson's article:

> . . . by suturing the central cut end of the sympathetic chain to the peripheral stump of the degenerating somatic nerve (Ballance). Under these conditions the preganglionic fibres of the sympathetic connector cells grow down the somatic path and establish relation with the striated muscle fibres, and these are thus brought again under the influence of the cortex.

I do not believe that Ballance,[14] in his monograph, which it was my privilege to review, intended even to imply that after sympathetic-hypoglossal anastomosis the muscle fibres now innervated by the cervical sympathetic had been brought under the influence of the cerebral cortex. He certainly does state that after sympathetic-hypoglossal suture the nerve "appears to function in the same normal manner as its predecessor"; but not only does he not infer that the cerebral cortex is responsible for this, but the statement contained in his account of experiment Number 3 indicates that the origin of the impulses now reaching the tongue, and indeed the very character of the contraction of tongue musculature, has been altered as a result of the operation. He says: "Stimulation of the pupillo-dilator centre in the hypothalamus was followed by tonic contraction of the muscles of the posterior half of the right side of the tongue". This observation by Ballance supports an identical observation made by Beattie, Brow and Long[15] in 1930. Ballance unfortunately did not stimulate the cortical hypoglossal representation on the appropriate side after the above nerve anastomosis, but the presumption is strong that had he done so he would not have observed any typical

tetanic contraction of tongue musculature other than that mediated by the very small degree of bilateral cortical representation present at the hypoglossal nucleus. Indeed, if the reverse procedure is adopted, namely hypoglossal-sympathetic suture, peripheral sympathetic effects, such as dilatation of the pupil *et cetera*, succeed stimulation of the appropriate cortical hypoglossal representation (Ballance, *loco citato*).

Other points on which I might have the temerity to disagree somewhat with Professor Wilkinson are of minor character and depend to some extent on one's personal judgement of the experimental or histological evidence available, so that I shall retire here with a final note of appreciation for Professor Wilkinson's excellent diagrams, many of which I shall find extremely useful.

In conclusion, it is of course difficult for those of us on whom falls the responsibility for the systematic instruction of students and the handing on of the results of recent research to our fellow graduates not to attempt to simplify our subject matter by too much abstraction. This procedure, while it facilitates absorption, at the same time sterilizes interest. In research, although rule is the substance and exception the sauce, the latter is essential if appetite is to continue.

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THE VOLUMETRIC MICRO-DETERMINATION OF SPERMINE IN SEMEN.

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Introduction.

IN 1678 Van Leeuwenhoek, the Dutch naturalist, discovered the spermatozoa in human semen. In his microscopical preparations, after they had stood for a little time, he also discovered glittering translucent crystals of lenticular shape, which he measured and depicted. A century later (1791) the French chemist Vauquelin again described these crystals occurring in semen which had stood for some hours, and considered them to be a hitherto unknown crystal form of calcium phosphate. Berzelius (1833) suggested that these crystals were ammonium magnesium phosphate. In the last third of the nineteenth and in the beginning of the twentieth century these crystals were referred to as "Böttcher's" crystals, because the German physiologist Böttcher rediscovered them (1865) and considered them to be a crystalline form of some type of protein.

Exactly 200 years after Leeuwenhoek's discovery Ph. Schreiner (1878) isolated Böttcher's crystals from semen and for the first time suggested their true nature as that of a phosphate of an unknown base, which subsequently was called Schreiner's base or spermine, as proposed by Ladenburg and Abel. Unfortunately the experimental details as given in Schreiner's paper were misleading and incorrect. Mostly for this reason, from 1878 up until about 1917, it was doubtful if any worker really isolated spermine phosphate from semen. Schreiner also pointed out that the presence of spermine is not specific to human seminal plasma, where it occurs in large quantities, but is also found in many other organs, which coincides with the observation of Böttcher that on the surface of old pathological specimens kept in alcohol, crystals appear which are identical with Böttcher's crystals. Schreiner also considered that the so-called Charcot-Leyden crystals, which resemble spermine phosphate in appearance and which are seen in the organs of leuchæmic patients and in the sputum of bronchial asthma, are identical with Böttcher's crystals. This assumption, however, has not yet been proven. In 1881 Fürbringer discovered Böttcher's crystals in prostatic secretion after the addition of phosphoric acid. The Russian physiologist, von Poehl (1898), without any scientific foundation, attributed great therapeutic potentialities to spermine phosphate. However, the once much advertised "Sperminum Poehl" was found to contain no, or only traces of, spermine.

Between 1923 and 1926 the chemical constitution of spermine was completely elucidated by the work of two groups of researchers working on this problem simultaneously, but independently, in London (Rosenheim and co-workers[1][2][3]) and in Greifswald (Wrede and co-workers[4][5][6]). By degradation and by synthesis it was shown that spermine or Schreiner's base was:

α-δ di (γ'-aminopropyl) amino-butane,

$NH_2CH_2CH_2CH_2NHCH_2CH_2CH_2CH_2NHCH_2CH_2CH_2NH_2$.

Spermine is an odourless substance. Its diphosphate forms the well-known lenticular-shaped crystals which Leeuwenhoek observed in semen 250 years ago. With picric acid it forms a highly insoluble tetra-picrate, which salt has been made use of in forensic medicine in the so-called Barberio test for the detection of seminal stains.

On pharmacological examination spermine proved to be of somewhat similar properties as cholin.

Small doses, that is, 0·1 milligramme per kilogram of body weight, given intravenously to rabbits, increase the blood pressure slightly. After larger doses the blood pressure is reduced. With comparatively very large doses the blood pressure falls very markedly; but as much as 40 milligrammes have no grossly visible influence on the rabbit, and the lethal dose was found to be above 60 milligrammes.

FIGURE I.

Typical crystals of spermine phosphate observed in semen forty-eight hours after ejaculation. The other material seen represents mostly disintegrating spermatozoa.

In higher animals, males as well as females, the presence of spermine has been demonstrated in practically every organ. It was further found to be present in yeast in appreciable amounts (0·01 milligramme per 100 cubic centimetres). Fæces contain traces of the base; but Rosenheim and others could not discover it in ox blood, cow's milk, hen's eggs, and in semen from bulls, and I could not discover it in semen from horses. For preparing large amounts of spermine salts the pancreas has usually been employed because it furnishes the highest yield of the easily accessible tissues. About 0·2 to 0·4 gramme of the base is obtained from one kilogram of bovine pancreas; but, as pointed out by Harrison,[7] the gland which usually gives by far the greatest yield of spermine is the human prostate, and he suggested that the spermine of semen is probably mainly, if not entirely, derived from the prostate. This author also worked out a gravimetric method for the approximate determination of the spermine in a single organ or a single specimen of semen.[8]

In connexion with some work on sex hormones I became interested in the micro-determination of spermine in semen. However, the method worked out by Harrison appeared to be somewhat lengthy and to require comparatively large amounts of semen for the purpose of the investigation planned. An attempt was therefore made to determine the spermine volumetrically immediately after its precipitation with picric acid, by titrating the picric acid content of the precipitate with methylene blue by a procedure described some time ago.[9]

Procedure.

To every cubic centimetre of semen three cubic centimetres of 5% trichloracetic acid solution are added while being stirred, care being taken to break up into small particles the precipitated lumps of protein. The mixture, after having stood for at least two hours, is centrifuged at high speed for about half an hour. Then a measured amount of the supernatant fluid, which should be clear, is transferred to another centrifuge tube, and calcium carbonate is added till it is no further dissolved by the acid present. Afterwards for every three cubic centimetres of filtrate, one cubic centimetre of a 0·1 N calcium picrate solution is added. The cloudiness which appears immediately after adding the calcium picrate is dissolved again by warming gently in a water bath at about 70° C. The tube is then allowed to cool and is transferred to an ice-box, where it is kept overnight. Spermine picrate is precipitated as a fine granular sediment, which can easily be separated from the mother liquor by centrifuging as well as by filtering off. After draining off the supernatant fluid, the precipitate of spermine picrate is washed with 0·5 cubic centimetre (for three cubic centimetres of filtrate) of water, then twice with one cubic centimetre of alcohol. The last washing should be pale yellow in colour, such as that of a solution of spermine picrate in alcohol, or further washing will be necessary. The precipitate is now ready for titration, and it may be transferred to a separatory funnel containing chloroform, with the aid of hot water or hot pyridine. Otherwise one may add 0·001 N methylene blue solution directly to the precipitate, which has been stirred up in some water. Methylene blue picrate is precipitated in dark flakes and further methylene blue is added till the well mixed fluid mixture has a distinct bluish appearance. One then transfers the whole of the mixture to the separatory funnel containing chloroform, and washes the tube with several lots of hot water. The titration of the spermine picrate is the same as that described for other picrates on previous occasions.[9][10] The methylene blue picrate formed is extracted with a volume of chloroform equivalent to three or four times that of the aqueous layer, and then more 0·001 N methylene blue solution is added till the aqueous layer is distinctly blue. Before renewing the chloroform it is advisable to let stand for about half an hour, because some small particles of spermine picrate may not have been dissolved before the end point has been reached, on account of their slow reaction with the very dilute methylene blue present. The chloroform is then renewed and, after repeated extraction, the end point is indicated by the appearance of a permanent light blue colour in the aqueous layer.

Since the spermine base is soluble in water as well as in chloroform, a part of it may be recovered to a large extent from the aqueous layer after terminating the titration by the addition of calcium picrate. On adding di-ammonium phosphate and alcohol to the aqueous layer the typical crystals of spermine phosphate will separate out on standing.

Discussion.

The principle of the method of Harrison[8] as applied to semen consists in the precipitation of the proteins and spermine phosphate present with alcohol. Then the precipitate is extracted with 2·5% trichloracetic acid and the spermine present in the filtered extract is precipitated with saturated aqueous picric acid. The spermine picrate precipitated is dissolved with hydrochloric acid and reprecipitated as spermine hydrochloride by means of acetone. This salt of spermine is finally converted into spermine phosphate and weighed as such. By converting 0·92 gramme of spermine picrate first into the hydrochloride and then into the phosphate the author of this method experienced a loss of approximately 10%, an error which may be considerably increased when dealing with much smaller quantities of spermine picrate, such as are obtained from one or a few cubic centimetres of semen.

In the method described in this paper the preliminary alcohol precipitation was found to be unnecessary if one used trichloracetic acid of 5% strength. To avoid contamination of the precipitate with picric acid, the precipitation is executed in a neutral medium with the highly soluble calcium picrate. The precipitation of the spermine present is complete because, after evaporation of the supernatant fluid to dryness, no further spermine could be discovered by the phosphate method. On the other hand, organic picrates other than spermine picrate are also precipitated to a certain extent. But most of them, on account of their greater solubility, are readily removed by washing with water and alcohol. The solubility of spermine picrate in water of 20° C. was found to be 0·021%, and in alcohol 0·0033%. One may also expect potassium to be precipitated with the spermine picrate. However, according to Slowtzoff,[11] the concentration of potassium in semen is only about 16 milligrammes per 100 cubic centimetres. Furthermore, the solubility of potassium picrate is greater than that of spermine picrate. In fact, no appreciable amounts of potassium were found in the washed precipitate, which may be assumed to consist mainly of spermine picrate, probably slightly contaminated with the picrates of other bases of similar solubility. Certain amorphous material, which is soluble in trichloracetic acid and which Goldblatt[12] considers to be proteose, is only precipitated to any considerable extent if one heats the reaction mixture over 70° C. This material, however, does not seem to form a stable compound with picric acid under the conditions described.

The titration with methylene blue is simple and accurate, as pointed out in previous communications.[9][10] Duplicate estimations on the same specimen of semen were found to agree within 3%, and spermine phosphate added to filtrates could be recovered quantitatively. If necessary, this determination could easily be executed on 0·5 cubic centimetre of semen.

Eighteen ejaculates obtained from two normal individuals have been examined for their spermine content by the method described. The values obtained (Table I) vary between 69 and 117 milligrammes of spermine, or, expressed as spermine phosphate, between 171 and 293 milligrammes, in 100 cubic centimetres of semen. Harrison performed six determinations on two individuals and obtained values of from 63 to 268 milligrammes per 100 cubic centimetres of spermine phosphate. Therefore, the values reported in this paper are considerably higher than values obtained by Harrison. They agree better with the result obtained by Rosenheim[1] by steam distilling semen (280 milligrammes of spermine phosphate per 100 cubic centimetres).

TABLE I.
Spermine Content of Human Semen.

Date (1935).	Spermine. Milligrammes *per Centum.*	Spermine Phosphate. Milligrammes *per Centum.*
Individual *A*, aged 34 years—		
June 22	102	256
July 5	71	180
8	69	173
11	81	203
15	84	210
19	93	233
25	81	203
28	117	293
August 2	79	198
6	99	248
12	103	258
19	96	240
Individual *B*, aged 26 years—		
July 2	88	220
15	84	210
23	86	219
26	77	193
31	114	285
August 9	70	175

Since the testes contain only about one-tenth of the spermine present in the prostate, Harrison considered the prostate to be probably the main source of the spermine present in semen. However, as mentioned before, Harrison found great variations in the spermine content of different samples of semen, and even more so in different individual prostates. From his findings he is inclined to presume that the quantity of spermine present in prostates, as well as in semen, is fortuitous, and any excess of spermine present in the body in general is excreted by the prostate. But the evidence for Harrison's hypothesis that the spermine in the prostate and in semen is simply a waste product in the course of excretion seems inconclusive. It is stated that in general the female body contains somewhat the same amount of spermine as the male. In the absence of any information regarding the presence of spermine in the excretions of the female it is not clear how this base is lost from the tissues in this instance. Moreover, Harrison's findings on prostates may not represent the true spermine values present in the normal living person, since the prostates were obtained from cadavers which showed various forms of pathological change. On the other hand, the observations on fresh semen reported in this paper do not show the same amount of variation as in Harrison's case. It is therefore sug-

gested that a specific function of the spermine present in the prostate and semen may still be discovered, in spite of the fact that up till now no such function has been proved.

Summary.

A simple volumetric micro-method has been described for the determination of spermine in human semen. From a neutralized trichloracetic acid filtrate the base is precipitated as spermine picrate, the picric acid content of which is determined by titration with methylene blue.

The results obtained in 18 specimens from two normal individuals vary from 69 to 117 milligrammes per 100 cubic centimetres of spermine, or 173 to 293 milligrammes per 100 cubic centimetres of spermine phosphate, with a mean of 89 and 222 milligrammes per 100 cubic centimetres respectively.

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Reports of Cases.

FOREIGN BODY IN THE STOMACH.

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P.D., AGED fourteen years, had a history of swallowing a large round-headed pin on Sunday night, three and a half days previously. At the first screen examination a foreign body was observed in the epigastrium near the mid-line, and a skiagram showed it to be a round-headed pin, with the point leading upwards. A small quantity of barium meal was given, and it was thought that the head of the pin was still within the lumen of the stomach, right at the pyloric ring; but the shaft of the pin was obviously outside the viscus. Skiagrams were taken in two different planes, and the relationship between the pin and the pyloric ring remained constant. I thought it necessary, however, to make quite certain that the object was not in the transverse colon. The patient was therefore brought back for a further examination four hours after the first one. At this time a trace of the contrast medium remained both in the stomach and in the duodenum. The relationship of the foreign body to these parts remained the same as at the morning examination. In addition, part of the contrast medium had gone on into the transverse colon, and this was seen to be lying a considerable distance below the foreign body. I therefore reported that the head of the foreign body was retained at the pyloric ring and that the point and shaft had penetrated the wall of the stomach. This finding was confirmed at operation five hours later.

It was suggested that the pin should be cut off close to the head and the latter "milked" into the duodenum and allowed to pass in the natural manner; but as the pin had penetrated the posterior wall and was surrounded by much omentum, Dr. Edye decided to open the stomach and remove the foreign body intact.

Comment.

Penetration by a foreign body of the gastro-intestinal tract is, in my experience, very rare. What probably happened in this case was that, just as the point of the pin reached the pylorus, it became caught in a fold of the mucous membrane at the identical moment when a peristaltic wave reached the head. Each succeeding contraction pushed the point and shaft further through the stomach wall.

Acknowledgements.

I am indebted to Dr. R. A. Eakin and Dr. B. T. Edye for permission to publish these notes.

A CASE OF UNDESCENDED TESTES SUCCESSFULLY TREATED WITH "ANTUITRIN S".

By CLIVE SIPPE,

Brisbane.

ABERLE and Jenkins,(1) Kunstadter and Robins,(2) and Webster,(3) among others, have reported the successful treatment of undescended testes by the use of pregnancy urine extracts. Webster reported eleven cases treated with "Follutein" (E. R. Squibb and Sons). He used an initial dose of 25 rat units, increasing by 25 units daily till a 250 rat unit dose was reached. This was given daily for two weeks. In ten of the eleven cases descent of the cryptorchid testes occurred during the period of treatment. The ages of the patients ranged from five to twenty-six years, and dosage from 1,500 to 5,000 rat units.

It was considered that the following case should be reported, as the treatment seems worthy of trial before surgical measures are adopted.

The patient, a male, aged ten years, was first seen on August 15, 1935, on account of enuresis. At the same time the father pointed out that neither testis was in the scrotum. On examination the scrotum was small and undeveloped. The right testis was just inside the inguinal canal and could be pushed nearly into the scrotum. The left was not palpable. Further examination did not reveal anything of note. The patient was a bright, active child, slightly undersized. As the right testis appeared mobile, it was decided to treat the condition with an extract of pregnancy urine ("Antuitrin S", Parke, Davis and Company). Large doses were employed, as advised by Webster. Treatment was instituted on August 22, 1935.

On September 3, 1935, it was noted that both testes were descending towards the scrotum. On September 8, 1935, seventeen days after treatment had commenced, when 1,950 rat units had been administered, both testes were in the scrotum. At this time there was a complaint of some pain along the inguinal canals. Treatment was suspended and the pain quickly subsided. One month later

both testes were still in the scrotum, which was becoming enlarged. The treatment made no difference to the enuresis, which is being treated as a separate entity.

References.

(1) S. B. D. Aberle and R. H. Jenkins: "Undescended Testes in Man and Rhesus Monkeys", *The Journal of the American Medical Association*, Volume CIII, August 4, 1934, page 314.
(2) R. H. Kunstadter and L. S. Robins: "Effect of Extract of Pregnancy Urine on Hypopituitrinism in the Male", *Journal of Pediatrics*, Volume IV, June, 1934, page 774 (abstracted in *The Journal of the American Medical Association*, Volume CIII, August 11, 1934, page 445).
(3) B. Webster: "Effect of Anterior Pituitary-Like Principle from the Urine of Pregnancy on Undescended Testes in Man", *The Journal of the American Medical Association*, Volume CIV, June 15, 1935, page 2157.

Reviews.

INFLUENZA.

D. AND R. THOMSON have in a second weighty volume completed their study of influenza.[1] This volume deals particularly with the complications and sequelæ, bacteriology of influenzal pneumonia, pathology, epidemiology, prevention and treatment. So monumental is this work that references to the literature occupy 101 pages, and a mere list of authors quoted in the text takes 22 pages of double columns. One can well believe the authors when they say that "the task of compiling this very large monograph on influenza has been excessive", and that it is their intention to rest for a few years from the ceaseless strain involved in compiling these volumes.

Though the name "influenza", probably of Italian origin, was first used in England in connexion with the epidemic of 1743, there is good reason to believe that epidemics can be traced back to the thirteenth and fourteenth centuries. "There is no doubt about the antiquity of influenza." Sweeping over continents in an incredibly short space of time, affecting and destroying millions of lives, this disease has come to be regarded as the greatest pestilence of our time, comparable with the plague in the seventeenth century. It is not definitely known what is the relationship between endemic or sporadic influenza and pandemic influenza. The clinical features are so protean that each new pandemic is apt to be regarded as some new disease. A bacteriological diagnosis is not yet available in practice in spite of recent advances. The prognosis largely depends on the presence or absence of pulmonary complications. "There is no doubt that the filter-passing virus theory of influenza . . . would appear almost an established fact, in which case Pfeiffer's bacillus, pneumococci and streptococci must be regarded as important secondary organisms . . . which would explain the diversity and prevalence of the secondary pneumonic inflammation so characteristic of influenza." The most satisfactory demonstration of an influenzal virus has been the transmission of a fever and nasal catarrh to ferrets by instillation of filtered throat washings from human cases, and there is evidence that the virus of human-ferret influenza is somewhat closely related to that of swine influenza. It is impossible to review shortly and adequately this encyclopædic monograph. Every conceivable aspect of the disease is discussed. It will suffice to mention some of the more interesting headings of sections: incidence of types of pneumococci in influenza-pneumonia, staphylococcal suppurative pneumonia complicating influenza, meningococcus bronchopneumonia complicating influenza, similarity of the respiratory complications in influenza to those produced by lethal war gases, ocular complications, affections of the peripheral nerves, psychoses of influenza, meningitis, epidemic encephalitis in relation to influenza, cardiac and circulatory complications of influenza (19 pages), gastro-intestinal influenza (12 pages), skin rashes (20 pages), the effect of influenza on pregnancy and labour, pulmonary tuberculosis and influenza (17 pages), pathology of influenza (100 pages), epidemiology (70 pages), modes of transmission (17 pages), vaccine prophylaxis and therapy, serum prophylaxis and treatment, preventive measures against influenza epidemics (83 pages). It will be seen that this monograph, Part II, in conjunction with Part I, previously reviewed in these columns, forms a mine of information and a valuable reference work on "infective disease number 1."

[1] "Annals of the Picket-Thomson Research Laboratory", Volume IX, Monograph XVI, Part I: Influenza, by D. Thomson and R. Thomson; 1933. London: Baillière, Tindall and Cox; America: The Williams and Wilkins Company. Demy 4to., pp. 656, with 28 plates. Price: 42s. net.

DERMATOLOGY.

R. L. SUTTON, senior and junior, are to be congratulated on the ninth edition of their text book, "Diseases of the Skin".[1] It forms a vast mine of dermatological information, well and copiously illustrated by photographs and by coloured plates. These coloured plates are, as usual, poor and the red element has been over-emphasized.

The general practitioner would be greatly helped in his diagnosis of the commoner dermatoses by the excellent descriptions given. The lines of treatment advocated are sound, internal remedies being placed in a minor rôle and more attention being paid to external remedies. Complete formulæ for the dispensing of the many applications advised are given in both the metric and, shall we say, imperial units. No attempt has been made to quote prescriptions for external applications, such as lotions on a basis of percentage of drugs used.

In the preface to the eighth edition which is included, reference is made to the lack of exact information in regard to the various forms of radio-therapy. The authors prefer not to give these details, as they rightly claim that these forms of therapy should be employed only by those who have received adequate training. This lack of detailed information is a serious loss to the dermatologist; however, he is compensated by the extraordinary wealth of references provided to the literature. These references are most up to date, many being for 1934. It is doubtful whether any other text book on dermatology in English contains such numerous and good descriptions and illustrations of the rarities of dermatology. We have tried to fault the book in this matter and have failed.

The scheme of the book is on a well organized basis, and although every dermatologist has his own ideas on the classification of the various dermatoses, none can complain of the general arrangement. The ever-present and increasing common condition of occupational dermatitis receives considerable attention and much sound advice as to prophylaxis and treatment is given. No mention is made in the section on impetigo of the efficient modern method of treatment by occlusive dressings of sticking plaster, but a wise word of warning as to the use of strong concentration of ammoniated mercury is given. A most useful classification of various drugs which may at times, and in susceptible individuals, cause skin eruptions is given, together with notes as to the type of eruption produced by individual drugs.

Senile and seborrhœic keratoses are considered together, but dissociated from the often concomitant squamous and basal celled epitheliomata. In the ætiology of these conditions the effects of sunshine as a causal factor do not receive sufficient attention.

We would deprecate the use of caustic agents, such as Bougar's paste, in the treatment of squamous celled epitheliomata.

Full descriptions and treatment of the various forms of fungus infections are given. The sections on the disorders of the hair and nails alone make the possession of the book desirable to the dermatologist.

[1] "Diseases of the Skin", by R. L. Sutton, M.D., Sc.D., LL.D., F.R.S., and R. L. Sutton, junior, A.M., M.D., L.R.C.P.; Ninth Edition, revised and enlarged; 1935. St. Louis: The C. V. Mosby Company; Melbourne: W. Ramsay. Royal 8vo., pp. 1433, with 1,310 illustrations and 11 coloured plates. Price: 75s. net.

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A SENSE OF VALUES.

If we say that a man has a sense of values, we infer that he shows discrimination, that he prefers one attainment or quality to another and will, if need be, dispense with the second to hold the first. But we imply more than this—we suggest that his choice is wise, that he chooses as we would choose. Almost every man, though he may not know it, has a goal, an end in life; and he values above other things those that will subserve that end. Possibly, of course, some of the things in which he delights may be ends in themselves. One man attaches most importance to money; his whole life is spent in making more and yet more money. He may like to surround himself with the things that money can buy; perhaps he thinks that money will give him power; he may, though such a person must be rare, look on money as a trust to be administered by him for the good of humanity. Another man may think of nothing but achieving a reputation for skill in his professional work or in his play. To such a one anything that will not help him to aquire skill or that will keep his prowess from being known will be without value. Yet another may glory in the fierce light of notoriety—he will set the stage with this end in view and will spurn everything that does not help to make the setting complete. A man values something because he takes joy in it or because he thinks it will make him happy; and probably there are as many types of happiness as there are types of men. Happiness is obviously emotional and as such is dependent on a state of mind; the state of mind is good or bad as it does or does not give rise to lasting happiness. Though contentment and peace of mind may be regarded as a happy state, real happiness implies something more active; there must be a sense of enjoyment, and happiness in its most exalted form would be described as ecstacy. We are thus dependent for happiness on what we value most, and a sense of values may be described as that which leads to a good state of mind.

If we grant that a sense of values will lead to a good state of mind, we must be prepared to name those things that we think desirable, and we must know why we pursue them. What appeals to a man will depend largely on his philosophy of life. Life is many-sided; it should be lived to the full. He lives the fullest life who "feels himself a citizen of the universe, enjoying freely the spectacle that it offers and the joys that it affords, untroubled by the thought of death because he feels himself not really separate from those who come after him". A man who lives a full life does not necessarily indulge himself with everything that the world has to offer; while he shows discrimination, he will satisfy most of his varying moods. If he feels himself to be a "citizen of the universe", if he has a cosmic sense, however small, he will devote himself to things of the spirit rather than to things of the body. Not that he will neglect the body. To him who lives a full life the things of the body will be supplementary to the things of the spirit. Such a man will use freely the avenues of the senses, but he will close the avenues in certain directions and open them in others, directing life continually by the effort of his will to its higher end. Such a man will see in

the world around him, in trees, in rocks, in running streams, and in all that is beautiful an expression of the great spirit of the universe. By the great masters of painting, music and sculpture he will be lifted out of himself, and he will feel impelled more and more to the pursuit and contemplation of their works. Even in his human relationships he will tend to be like the poet who, in painting "Her Portrait", sang:

> How should I gauge what beauty is her dole,
> Who cannot see her countenance for her soul,
> As birds see not the casement for the sky?
> And, as 'tis check they prove its presence by,
> I know not of her body till I find
> My flight debarred the heaven of her mind.

In short (using the term heaven in its esoteric sense) he will be fulfilling the command: "Lay up for yourselves treasures in heaven, where neither moth nor rust doth corrupt, and where thieves do not break through nor steal". Eventually he will be like the man described by Olive Schreiner in her remarkable novel "The Story of an African Farm", who saw a sheen, a shimmer, a reflection in the water, of "a vast white bird, with silver wings outstretched, sailing in the everlasting blue", whose name was Truth. He set out to climb the almighty mountains of Dry-facts and Realities in pursuit of her, slipping and even falling in his ascent, but urged ever upwards by a knowledge that she was somewhere above him and that she alone could satisfy his needs. He found her not, but as he lay dying a silver feather from the wing of the white bird fluttered down from the sky and he died holding it. The happiness of one who with a balanced and well-stored mind sets out to find truth will be of rare moments only; he will suffer much but he will never forsake his quest.

Since a sense of values is a desirable possession, and since certain qualities and attainments which would appear to many people to be without value are the most to be prized, we naturally ask ourselves how men and women may be brought to accept this valuation, though to urge its acceptance may be a counsel of perfection. Clive Bell has written that it is useless to tell a man that certain keys will unlock the gates of Paradise unless he is given a taste for Paradise. This, he adds, is what education can do. He thinks that one of the great problems of humanity will be solved if boys and girls can be made to realize that the delight of being alone in a bed-sitting room with an alert, well-trained, well-stocked mind and a book is greater than that of owning yachts and racehorses, and that the thrill of a great picture or of a quartet by Mozart is keener than that of the first sip of champagne. There is no doubt that were the young taught to value the intangible things that make for abiding happiness, they would acquire a stimulus to good living and high thinking and they would be able to build up within themselves reserves on which they could draw in times of need, and particularly when their years were advancing. Those who have grown to maturity without a sense of values will find it difficult to acquire; but by experiment, experience and selection they may gradually be able to form new habits and to discover fresh ways of thinking.

Current Comment.

DIET AND THE ONSET OF DIABETES.

THE activities of the Press and of radio are now so many-sided that very many of the aspects of health are freely exploited by them. That this is always due to a purely altruistic regard for the health of the multitude may perhaps be doubted; but medical practitioners are more and more frequently asked to give advice on the subjects that fall into the category of preventive medicine. Diabetes is one of the diseases about which such advice is sometimes sought; it is known that there is an hereditary type of diabetes, and the question is sometimes put: "What diet should he or she adopt in order to lessen the risk of contracting the disease?" Realizing that there are other factors, both economic and endocrine, that may play a part more important than diet, the medical practitioner may not stress unduly the importance of diet, but that it is important he must admit, and he must also give advice of some kind. Once, in the bad old days of severe carbohydrate restriction, he might have advised abstention from starches and sugars, even with lingering doubts raised by the successes of the potato and oatmeal diets. But now what advice will he give? He first must have some idea what diets are commonly adopted by those persons who actually become diabetics, that is, what food diabetics actually consume prior to the onset of their disease.

This question has been answered by H. P. Himsworth and E. M. Marshall in a recent inquiry into the subject.[1] It is known that the sugar tolerance of a healthy person is determined by his diet; it is also known that the tolerance of an established diabetic may be raised by the employment of a reasonably high carbohydrate diet. Thus a low carbohydrate/high fat diet impairs the glucose tolerance even of healthy individuals, whereas a high carbohydrate/low fat diet will improve it. This has been shown by Himsworth in another paper to be due to the variation of carbohydrate in the diet, and not *per se* to the variation of fat. The explanation of this is that the varying carbohydrate induces a varying insulin response from the pancreas, and, as Himsworth puts it, the change in glucose tolerance that occurs when a diet is raised in carbohydrate and lowered in fat, is due to a change in the sensitivity of the individual to his own insulin. If then the factor necessary to sensitize a susceptible individual to his own pancreatic insulin (that is, glucose) is lowered, his sugar tolerance may be impaired and the clinical picture of diabetes produced. Following this argument we should expect diabetics, prior to the clinical onset of their disease, to have taken diets relatively low in carbohydrate and high in fat. Himsworth and Marshall have put this hypothesis to the test. The time of appearance of the clinical syndrome of diabetes they adjudged by glycosuria, nocturnal frequency or local pruritus. These signs would be sufficiently reliable to indicate the time of onset in a person who was known to have become a diabetic, and the age incidence curves obtained in this inquiry corresponded with those described by Joslin and others. Normal controls of corresponding age and type were obtained from hospital in-patients, excluding those who suffered from any complaint affecting appetite or digestion. The diet was investigated by two methods: one a purely qualitative inquiry as to what dietetic changes, if any, had been made by the subject; the other quantitative, an attempt being made to assess the actual quantities of foodstuffs consumed. One of the authors being a hospital dietician, and the other specially interested in diabetes, the results of the inquiry may be taken as reliable. Their figures were submitted to mathematical analysis, and all care was taken not to suggest answers to the patients questioned. The authors found, rather to their surprise, that, irrespective of ages, the diabetics chose on the average a diet different from that of normal subjects. Summarizing their analysis, it was found that the majority of diabetics, prior to the onset of their disease, preferred diets containing an undue proportion of fat. Only a smaller number of diabetics preferred a diet containing excessive carbohydrate. The diets themselves were of higher caloric value than the controls, as might be expected. Not only did the diabetics express preferences as indicated here, but their actual diets before onset of the disease showed an excess of fat and a diminished carbohydrate as compared with the protein. It is suggested that the diminished carbohydrate was responsible for a progressive permanent impairment of the sugar tolerance and thus the insulin sensitivity of the individual. It should be remembered, therefore, that any advice offered to protential diabetics should be governed by a knowledge of the physiology of food absorption and utilization, and that the known factors controlling the production and activation of insulin should be borne in mind.

[1] *Clinical Science incorporating Heart*, Volume II, Number 1.

SYPHILIS AND BLOOD TRANSFUSION.

IT is perhaps an exaggeration to say that the operation of blood transfusion is surrounded by difficulties and perils of a major kind; but it is no overstatement of the case to remark that no other therapeutic procedure requires greater forethought as to the problems involved, nor greater care in the technique employed. As an instance, only comparatively recently in the march of medicine have the conditions making for safe blood grouping been thoroughly understood. Apart from these considerations, Hugh J. Morgan[1] has lately given consideration to the factors which appear to govern the transmission of syphilis by blood transfusion. He was driven to make this inquiry by the regrettable fact that a colleague found himself involved in a law-suit through an accident of the kind.

Such transmission of syphilis was first noted by Fordyce in the year 1915, and Morgan has been able to collect sixteen similar instances. In all of these the disease appeared in the blood recipients in the form of characteristic "secondary" lesions after an incubation period varying between one and three and a half months. As to the donors concerned, nine out of eleven who could be traced were found to have been suffering at the relevant time from either primary or secondary syphilis, and one unfortunate developed a primary chancre four days after giving his blood. One instance is recorded of a donor who contracted the disease from a recipient, a tragedy resulting from a changing of the cannulæ during the course of the operation. Nevertheless, the evidence, both experimental and clinical, seems to Morgan to show that the blood of an individual with chronic latent syphilis will not induce the disease in a blood recipient. Apparently this has been proven true of rabbits as well as of man; and Tzanck, working with Werth in 1930, produced a donor who, whilst suffering from latent "sero-negative" syphilis, gave blood to eighteen recipients without harmful results to the latter. The important qualification has to be remembered, however, that pregnant women with chronic forms of syphilis are capable of transmitting the disease; in such women only and in patients with active primary or secondary lesions is the virus present in the blood. The medico-legal importance of the subject is enormous.

[1] *The American Journal of the Medical Sciences*, June, 1935.

Abstracts from Current Medical Literature.

THERAPEUTICS.

Action of Oil of Peppermint on Gastric Activity.

WORKING on the hypothesis that the pain of peptic ulcer is due to a local ischæmia and asphyxia resulting from depletion of the vascular bed in and about the ulcerated area, Jacob Meyer *et alii* (*Archives of Internal Medicine*, July, 1935) used an essential oil to cause a local hyperæmia. The first investigations on this line were into the effects of ingestion of oil of peppermint on the secretion and motility of the stomach in man. The authors' first test was to introduce one to two cubic centimetres of oil of peppermint (U.S.P.) with 10 cubic centimetres of normal saline solution through a Rehfuss tube after the withdrawal of two to five samples of gastric juice at ten minute intervals from the fasting stomach of nine patients with gastric ulcer. Charting their results, they found that in the majority a considerable reduction of free acid occurred; control tests with 10 cubic centimetres of normal saline solution showed no influence on the free acidity. Using 100 cubic centimetres of a 7% solution of ethyl alcohol as a secretagogue, they obtained a good response of free acid; the administration of the alcohol with olive oil also gave a high free acid content, whilst the simultaneous introduction of oil of peppermint with the alcohol inhibited the secretion of free acid. The combined acid did not show any increase to account for the disappearance of free acid; there was an increased volume of secretion. Histamine being a still stronger gastric secretagogue, a subcutaneous injection of 0·35 milligramme of histamine acid phosphate was given simultaneously with the introduction of two cubic centimetres of oil of peppermint through the Rehfuss tube. In all except one case, in which a hyperthyreoid state existed, there was a diminution of secretion of acid in all tests after the oil of peppermint was given, even if higher acid levels were accounted for in the controls for the histamine tests. The administration of oil of peppermint thirty minutes after the secretagogue failed to demonstrate any significant reduction of the free acid. Menthol, one of the main constituents of oil of peppermint, when given in the dosage of 0·5 gramme in 100 cubic centimetres of 7% alcohol, gave negative results. There was no increase in the secretion of visible mucus to explain the effect of the peppermint. With regard to the motility of the stomach, the tests carried out show no change with doses under 10 cubic centimetres and inhibition of motility with doses above 10 cubic centimetres. These results are somewhat at variance with others carried out in the same laboratory, normal persons showing a considerable decrease in the emptying time of the stomach after a barium sulphate meal *plus* two cubic centimetres of oil of peppermint. The mechanism of the depressing action of oil of peppermint on gastric acidity has not yet been satisfactorily explained. Various theories are commented on by the writers.

"Gynergen" in Migraine.

THE use of ergotamine tartrate ("Gynergen Sandoz") for the treatment of migraine was first reported in 1926 by Maier. Various reports have been since published, and William G. Lennox and Theodore J. C. von Storch (*The Journal of the American Medical Association*, July 20, 1935) give their experiences in a series of 120 patients. The patients all suffered from severe periodic headaches with one or more of the following satellite symptoms: hemicrania, nausea or vomiting, visual disturbances, vasomotor disturbance, and malaise. Other methods of treatment had failed before the use of ergotamine tartrate. Twenty-three of the series were males. The drug was given by various routes: subcutaneous, intravenous, intramuscular and oral. Of the whole group, 89% experienced abrupt and complete cessation of the headache with the initial use of ergotamine, thus showing that in this drug the physician possesses a valuable non-sedative substance which is more useful than any other single therapeutic measure. It seems to be specific, or nearly so, for the migrainous headache. Results of repeated treatment were also very encouraging, for the majority of patients responded to subsequent injection, as they did to the initial trial; but it was noted that headaches aborted by ergotamine tended to recur at shorter intervals, especially in the earlier months of treatment. A sense of fatigue and lassitude is often complained of, whilst nausea and vomiting occur more frequently; paræsthesias, muscular pains, and sense of substernal oppression are other symptoms reported. Patients with arterial disease must be treated cautiously, as the administration of the drug tends to raise the blood pressure. Pregnancy is not a contraindication. The average dose required is 0·5 milligramme, but a second similar dose may be necessary; this is the amount for the parenteral route. If the drug is being administered orally, a much larger dose is required, as only 30% is absorbed. At the onset of the headache two to five milligrammes may be administered and one to two milligrammes given at hourly intervals until nine to ten milligrammes have been taken; two hours or more may elapse between ingestion and relief. It may be possible to lessen the severity of the attacks if the time of their onset is predictable and treatment is instituted; but, although ergotamine is useful in aborting the individual attack, no effort should be spared to find the cause or causes of the condition. There is no satisfactory explanation of the mechanism of action of this substance in relieving migrainous headaches.

Artificial Pneumothorax in the Treatment of Lobar Pneumonia.

THE induction of artificial pneumothorax is a measure which has recently been added to the list of therapeutic agents for the treatment of lobar pneumonia. There are many factors which must be taken into consideration before instituting this form of therapy in any particular instance, and Jesse G. M. Bullowa and Edgar Mayer (*The Journal of the American Medical Association*, July 20, 1935) take the opportunity of pointing out some of the hazards associated with this procedure. Artificial pneumothorax must be induced early in the disease, as it is obviously impossible to cause collapse of the consolidated lung, and this may delay the use of other treatment, serum therapy for example. Collapse of uninvolved lung may aggravate the dyspnœa in a patient whose demand for oxygen is already increased by reason of fever and the admixture of oxidized and unoxidized blood; the affected lobe may remain inflated while the uninvolved portion may be collapsed. The introduction of air into the inflamed pleural cavity presents conditions favourable to the development of fluid that may become purulent. Separation of the pleural surfaces precludes the localization of empyema, should it occur as a spontaneous complication. Traumatic rupture of the lung and air embolism have occurred. Infected mucus may be forced into the other lung, with the development in some cases of a contralateral pneumonia, notwithstanding the induction of artificial pneumothorax. Elderly people with reduced vital capacity, or those with cardio-vascular diseases have not done well. Patients with bacteriæmia, either early or late in the disease, do not respond favourably. It is pointed out that blood invasion is of great importance as far as prognosis is concerned; it has not been shown whether artificial pneumothorax can prevent this. The alteration in blood volume flow through the collapsed lung is recognized, and it is also probable that there is a reduction in the lymph drainage from the collapsed lung, but what part these or any other physiological alterations may play in the healing process, we do not know. The conclusion is arrived at that there is insufficient evidence to warrant the use of artificial pneumothorax in the treatment of lobar pneumonia, except in large hospitals amply equipped for radiographic and pathological studies; also the treatment should not be employed by those inexperienced either in the treatment of pneumonia or in the use of artificial pneumothorax. It is still in the experimental stage.

NEUROLOGY AND PSYCHIATRY.

Spinal Tumours in Childhood.

WALLACE B. HAMBY (*The Journal of Nervous and Mental Disease*, January, 1935) presents an analysis of the literature and the report of a case of spinal ependymoma. The cases analysed in this series do not include hydatid cysts, spinal extensions of the intracranial tumours, the granulomata and other inflammatory lesions. Of the thirteen so-called "hour-glass" tumours of the spine found in children, five were sarcomata. In the whole series of 100 the most frequently occurring spinal neoplasms were sarcomata, gliomata, lipomata, dermoids, chloromata and neurinomata. Meningiomata and chloromata occur only late in the period of childhood. The characteristic tumours of infancy are lipomata and dermoids.

Hypophyseal Cachexia.

LEWIS GUNTHER AND CYRIL B. COURVILLE (*The Journal of Nervous and Mental Disease*, July, 1935) give a lengthy and extensive report of a case of Simmond's disease, a rare condition associated with atrophy of the *pars anterior* of the hypophysis. The patient was a Mexican woman of forty years, who came to the hospital complaining of weakness and cachexia. The onset was insidious. At the time of admission to hospital she had symptoms relating to insufficiency of the adrenal cortex, such as weakness, low blood pressure, pigmentation of the skin and hypoglycæmia; symptoms and signs of hypothyreoidism and myxœdema, such as intolerance to cold, dryness of the skin, loss of hair and a low basal metabolic rate; loss of the secondary sex characteristics, such as the loss of axillary and pubic hair, atrophy of the breasts, genitalia and the reproductive organs. The patient, becoming further cachectic, finally died and a *post mortem* examination was conducted. This was very extensive and involved a microscopic study of all the body tissues. Summarized, this examination revealed: atrophy of the anterior lobe of the hypophysis, polyglandular atrophy, affecting thyreoid, adrenal and ovarian glands; atrophy of the right *bulbus oculi* with degeneration of the right optic nerve and tract; fibrosis of the lungs, probably tuberculous in origin, and general diminution in the size of all the organs. Differential diagnosis included arsenical poisoning, myxœdema, Addison's disease, pernicious anæmia and carotinæmia.

Cerebro-Spinal Fluid in Brain Tumours.

CLARENCE C. HARE (*Bulletin of the Neurological Institute of New York*, March, 1935) sets out to study change in the spinal and ventricular fluid in cases of brain tumour which were verified subsequently by autopsy. Of the 218 cases studied, the fluid was obtained by the lumbar route in 186 and by ventricular puncture in 79. The author is of opinion that a study of the ventricular fluid is of little value in differential diagnosis of cerebral neoplasm from other brain diseases. Increase of protein and of globulin is the most frequently noticed change in fluids associated with cerebral tumour. The author gives percentages of pathological increase associated with the various varieties of neoplasm. He finds that changes in protein and globulin of fluid removed by ventricular puncture are less frequent; but in supratentorial growths in one hemisphere the fluid tested from the lateral ventricle of that side was found often to contain a greater excess of protein and globulin than a specimen tested from the opposite ventricle. Greatest excess of protein and globulin in the lumbar fluid was noted in cases of multiform glioblastomata and in acoustic nerve tumours, in contradistinction to the protein excess in ventricular fluids which was found associated with multiform glioblastomata only. Pleocytosis was noted in only 8·6% of the cases studied. The main value of a chemical examination of the fluid is in indicating the probable pathological nature of the growth.

Pseudotumour Cerebri.

ALEXANDER SILVERSTEIN (*American Journal of Syphilis and Neurology*, July, 1935) reports the case of a patient with characteristic features of a brain tumour syndrome, in which necropsy failed to reveal a tumour. The patient, who was under observation for a considerable period, was subjected to clinical and biochemical tests. A review of the literature describing similar cases is published and conclusions are drawn therefrom. The author believes that there are certain cases which present all the classical features of brain tumour, but which are due to other cerebral pathological changes. In the case which he reports, histopathological examination revealed meningeal fibrosis, marginal gliosis and an old sclerotic process of the *cornu ammonis*. The author claims that the encephalogram may show either an absence of the cortical pathways or enormous dilatation of the channels. He also states that spinal drainage in a selected group of cases may result in prompt and permanent cure and should be tried before surgery is attempted. The condition of pseudo-tumour of the brain may begin with psychotic manifestations, which may simulate a true psychosis. In the light of his research, though the phrase pseudotumour is a poor one, it should be retained for such cases.

The Migraine Personality.

OLGA KNOPF (*The Journal of Nervous and Mental Disease*, September and October, 1935) confines her attention to a little known aspect of migraine—the personality of the patient. Many observers have denied the existence of a migraine personality. The author reviews the somewhat extensive literature on migraine. In her own study of thirty migraine patients the greatest emphasis was laid on the patient's psychic make-up before the onset of his illness. No distinction between the sexes was deemed necessary in the investigation of the structure of their personality. The author finds that a definite type of personality exists among migraine patients. They tend to be "goody-goody", very ambitious, reserved, repressed, sensitive, domineering, resentful, and to possess very little sense of humour. The genital phase adjustment in the women was incomplete. The structure of the personality played a part in the provocation of the illness, as also in the precipitation of the attack. Events could be found similar to those which precede the onset of a commoner neurosis or personality maladjustment, such as, for instance, the onset of menstruation, pregnancy and the gestation period. The author claims that an investigation of the personality make-up is essential in the proper investigation of a case of migraine and that more attention than heretofore must be paid to psychological readjustment when the patient comes to be treated for migraine.

Group Therapy in Psychiatry.

L. CODY MARSH (*The Journal of Nervous and Mental Diseases*, October, 1935) considers the treatment of psychoneurotic patients who cannot afford private treatment and who are thereby compelled to attend a psychiatric clinic. For these patients he advocates group therapy, which, he claims, has special advantages over individual treatment. It provides a kind of therapeutic compulsion, an educational and attractive set-up. Enthusiasms are engendered in the group which are not so prominent in private treatment, and the impersonality of the situation makes the patient more amenable to treatment. The author emphasizes the fact that psycho-neurotics should be regarded more as students than patients and that the group therapy is more an educational than a medical procedure. Considerable success in the group method was obtained with stammerers, and the author suggests the advisability of a group psychiatric approach to asthmatic, allergic, gastric ulcer and diabetic cases as a profound help to the physician who in an out-patient department has a number of such patients to attend to. It can scarcely be denied that the giving to patients of an insight into the psychological factors involved in various illnesses of which they complain is a valuable aid to their successful treatment, and in an out-patient department such a procedure would not only save a great deal of time, but would to a large extent prevent the manufacture of a large number of the hypochondriacal and chronic neurotic individuals who clutter the clinics of every large out-patient department at the present day.

British Medical Association News.

SCIENTIFIC.

A MEETING OF THE NEW SOUTH WALES BRANCH OF THE BRITISH MEDICAL ASSOCIATION was held at the Royal North Shore Hospital of Sydney on June 20, 1935. The meeting took the forms of a series of demonstrations by the members of the honorary staff. Part of this report appeared in the issue of November 23, 1935.

Orthopædic Conditions.

DR. S. H. SCOUGALL, DR. A. R. HAMILTON and DR. A. L. DUCKER, of the Orthopædic Department, demonstrated several patients as follows.

Manipulation of the Hip.

A woman, aged fifty-one years, had complained on March 13, 1935, of a low backache and pain in the left groin extending down the front of the left thigh into the knee, of about five years' duration. The pain had been improved by physiotherapy and by a chiropractitioner, but had recurred.

Examination revealed full function of the right hip, but a flexure contracture of about 30° of the left hip. Flexion, internal and external rotation of the left hip were all markedly limited and painful. X ray examination showed advanced osteoarthritis of the left hip, slight osteoarthritis of the right hip, and slight changes in both sacro-iliac joints. No obvious foci of infection were found.

On March 26, 1935, a manipulation of the left hip under general anæsthesia was carried out, and adhesions were broken down on external and internal rotation. After several weeks of physical therapy the patient had full flexion and full rotation, but still a flexure contracture. Pain had been considerably diminished. She was able now to put on her left shoe and stocking with comfort and ease, whereas previously this had caused great inconvenience.

Manipulation of the Sacro-Iliac Joint.

A woman, aged thirty-two years, had complained on May 26, 1934, of severe pain over the right side of the lower part of the back and the right hip region, following childbirth about eighteen months previously. All local treatment had given no relief. On examination there was pain over the right sacro-iliac region, increased by sacro-iliac movements, with a definite relief stance or sciatic scoliosis. No obvious foci of infection were detected. A manipulation of the back under general anæsthesia was performed. A loud thudding sound was heard—apparently the replacement of a subluxated sacro-iliac joint. The next day the pain was much less, and on June 12, 1934, there was complete freedom from pain.

Manipulation of the Feet.

A woman, aged fifty-three years, had complained of pain and tiredness in both feet of some years' duration. Other joints were free of pain. On examination there was severe pain on inversion of the right foot, less pronounced in the left. Marked grating of knees and shoulders was present. A manipulation of both feet was performed and snapping of adhesions was obtained on inversion. One week later the patient admitted greater ease in her feet than she had experienced for many years. Treatment was discontinued after about one month. At the time of the meeting the only disability was a mild anterior metatarsalgia, which was considerably relieved by metatarsal bars.

Manipulation of the Knee.

A woman, aged forty-eight years, had complained of a pain in the right knee since a fall five weeks previously. On examination external rotation caused a pain on the inner side of the knee. Other movements were painless. No grating and no swelling were detected. X ray examination revealed no osseous lesion. A manipulation of the right knee was carried out and a snap was felt on external rotation. One month later there was full range of painless movement of the knee joint.

Manipulation of the Wrist.

A woman, aged fifty-four years, had a Colles's fracture on November 27, 1934, and on March 8, 1935, still had pain and limitation of movement of her left wrist joint. A manipulation was performed, and treatment was discontinued about six weeks later with practically a full range of painless movement.

A male patient fractured the lower end of the right radius on February 27, 1935, and was treated in the usual manner. On April 17, 1935, he had practically full movement and was discharged. On June 7, 1935, he returned with a very limited and painful palmar flexion. One week later a manipulation of the left wrist under general anæsthesia was carried out, when practically full flexion was obtained. Since then the patient had had the usual physical therapy and at the time of the meeting had a full range of movement.

A Shoulder for Manipulation.

About four months ago a woman, aged fifty-nine years, fell and hurt her left arm. Since then she had never been free from pain, which had been getting worse, and limitation of movement was increasing. There were no obvious foci of infection, and physical therapy had merely aggravated the condition. X ray examination revealed no abnormality. The patient was apparently suffering from a periarthritis of her left shoulder joint. She was to have a manipulation of her shoulder under a general anæsthetic, followed by the use of an abduction splint for two to three weeks, and suitable physical therapy.

Osteomyelitis with Intercurrent Anterior Poliomyelitis.

One year ago a boy, aged five years, had an osteomyelitis of the lower quarter of the right femur, which was opened and pus was evacuated. The bone was cauterized and packed with vaseline gauze. The child made a slow convalescence, and at the end of nine months had reached a stage at which a small sinus was intermittently open. During this period there were several exacerbations of temperature, with local signs of swelling and redness. About the middle of April, 1935, the child again had a temperature of 39·4° C. (103° F.) and complained of pain in the affected limb. There were some signs of local infection in the bone at the site of the local lesion.

With recumbency the symptoms subsided and at the end of four weeks he was sent to Sydney for an X ray examination of the lower third of the right femur, which showed a definite sequestrum of moderate size lying superficial to the old area of infection. This was removed and the leg was encased in plaster, with the wound dressed in the Orr method. About one month later in the country the plaster was removed and ambulation was attempted. A drop-foot was then noticed and a more complete examination showed a widely spread degree of paresis of the whole right limb and the gluteal muscles on both sides, obviously due to intercurrent anterior poliomyelitis occurring in a sequence of exacerbations of his bone infections.

Lardaceous Disease Treated with Liver.

A woman, aged thirty-five years, single, who was born in Scotland but had lived in Australia since 1928, was admitted to hospital on January 4, 1934. She gave a history of pain in the left knee and left hip since about 1931. About twelve months before admission an abscess in the left thigh opened spontaneously and a sinus had persisted. She had had slight cough and sputum for about three years.

On examination there was practically no movement at the left hip; this region was very swollen and Alexandroff's sign was present. The left lower extremity was considerably shortened and a discharging sinus was present at the junction of the middle and upper thirds of the thigh on the outer side.

X ray examination on January 4, 1934, revealed complete absorption of the head and the greater part of the neck of the left femur, with some irregularities and decalcification of the upper part of the corresponding acetabulum

and upward displacement of the trochanter. After injection of lipiodol into the sinus an X ray examination revealed extensive ramification of the sinus. A diagnosis of tuberculosis of the hip joint was made.

On January 18, 1934, this patient was treated on a Jones abduction frame. On August 28, 1934, a plaster spica was applied with the object of allowing ambulation on crutches. About November 20, 1934, diarrhœa commenced; this occurred at intervals for several months and was considered by Dr. Cotter Harvey to be a manifestation of lardaceous disease, but no casts were found in the urine. In view of this complication, the spica was replaced by a Thomas hip splint, and on May 22, 1935, "Campolon" administration was commenced, resulting in complete cessation of diarrhœa.

It was explained that in view of the improvement of the waxy disease under liver therapy (Campolon), the prognosis as to life was fairly good. It was impossible to foretell the ultimate outcome of the local lesion, in view of the gross destruction of the head and neck of the femur and the loss of apposition of bone to bone and the presence of numerous discharging sinuses with their resultant secondary infection.

The points of importance to be noted were: (i) The gross destruction as a result of tuberculous infection and the lack of response of the hip disease to treatment. (ii) The rapid response of diarrhœa to liver therapy.

Osteomyelitis with Reconstructive Surgery.

A male patient, aged twenty-two years, was first seen in consultation in the latter part of 1932 with subacute osteomyelitis of both ilia, involving the hip joint and the upper end of each femur. At that time he was *in extremis*. Both hip joints were dislocated and the lower limbs were deformed. The back, thighs, and legs were covered with bed sores.

Beyond removal of several sequestra, nothing further was done at that time. The patient eventually recovered from the sepsis and then presented the following picture. Both hip joints were dislocated, the head of each femur having been absorbed and the great trochanter on each side being well up on each ala. The left thigh was in extreme flexion—adduction deformity. The knee was in flexion at 45° and the foot in severe equinus. A moderate range of movement was present at the pseudarthrosis of this side. The right thigh was in a corresponding degree of abduction and flexion and bony ankylosis was present between the upper end of the femur and the ilium. The knee on this side was also in flexion and several sinuses were present around the upper end of the right thigh.

The patient could not walk without the aid of crutches and even then had a crab-like gait, the toes pointing to his right and knees half right to his line of progression.

On November 12, 1934, under general anæsthesia, a Lorenz bifurcation of the left femur was carried out, the upper end of the lower fragment being thrust into the acetabulum and the flexion adduction deformity being corrected. Good union subsequently occurred and the patient now had a straight, practically painless leg.

On April 1, 1935, under general anæsthesia and in spite of the presence of two discharging sinuses, osteotomy of the right femur was performed below the area calculated to be infected. The abduction and flexion were corrected and a plaster spica was applied. There was no exacerbation of the local infection, as was feared might occur.

It was pointed out that the patient's function had been considerably improved by surgery. He would have great difficulty in sitting, and owing to the small range of movement at the left hip, it might be possible for him to dispense with crutches except on hills and rough ground.

This case, it was stated, demonstrated very clearly what happened when acute infection invaded the hip joint. The dislocations, subsequent deformities and most of the bed sores might have been averted by the use of a Jones frame in the acute stage of the disease. On such a frame the joint was put at rest and a great deal of the pain and resulting distress was prevented and nursing was considerably facilitated.

Transcervical Fracture of the Neck of the Femur.

A woman, aged seventy-one years, fell and injured her left thigh on December 26, 1934. She was taken to hospital, where an X ray examination showed a complete transcervical adduction fracture of the neck of the left femur. She had been convalescing from an arthrodesis of the ankle performed about five months previously. No active treatment of the fracture was undertaken, chiefly owing to the mental condition of the patient. She was somewhat confused and was not very anxious for treatment after the fracture. Nearly three months later, on March 12, 1935, there was considerable upward displacement of the shaft of the femur, with wide separation at the site of the fracture. The mental condition had improved, and with general ether anæsthesia, under X ray control, the fracture was reduced after the manner of Whitman; and, when the exact position was verified radiologically, the fracture was impacted with a weighty wooden mallet, and placed in a Whitman plaster. On March 16, 1935, she was transferred from the country to Sydney. The plaster was maintained almost three months, being removed on June 5, 1935. During this time her mental condition had become increasingly confused, though her physical condition remained reasonably good.

Her progress X ray reports were as follows. On April 15, 1935, there was no definite evidence of bony union; the position was satisfactory. On May 16, 1935, it was thought that bony union was taking place, but it was far from complete. On June 15, 1935, a fair amount of bony union was present.

The following extract from a book on fractures by Paul B. Magnusson was quoted:

> Cotton has advised an artificial impaction of the femoral neck. He performs this by pressing the fragments of the neck opposite each other by traction and internal rotation, placing a double layer of heavy felt over the trochanter of the injured femur with the patient firmly supported on the opposite side and then striking a heavy blow with a wooden mallet weighing about eight and a half pounds, the force being applied on the pad immediately over the trochanter. The blow is repeated several times if necessary, until there is a feeling of yielding beyond the mallet and the leg no longer rolls loosely into external rotation.

An extract from Böhler's "The Treatment of Fractures", fourth edition, was also quoted:

> Many people hold the opinion that old people with a fractured neck of the femur cannot obtain bony union, and therefore they refrain from any treatment and even from X ray examination. But it should be insisted that of all the fractures in the upper end of the femur, two-thirds involve the trochanters and are therefore benign. Only one-third involve the true neck of the femur, more frequently being near to the head (subcapital) than through the middle of the neck (intermediate or transcervical). The pertrochanteric fractures can usually be easily distinguished at the outset from the intracapsular or medial subcapital fractures of the neck of the femur. In the pertrochanteric fractures the leg is rotated outwards completely, so that the outer margin of the foot lies on the bed, while in the medial fractures of the neck outward rotation is only 45° to 60°.
>
> Pertrochanteric fractures make a good recovery at any age, with bony union and full function, if properly treated, *i.e.*, by continuous traction in a position of abduction and slight inward rotation, maintained for a sufficiently long time.
>
> In the medial subcapital or intracapsular fractures two varieties are sharply distinguished from the point of view of prognosis. The common type (about 80%) is the adduction fracture with coxa vara and outward rotation of the leg. There is an angle between the fragments open inwards and backwards. Usually this fracture is not impacted, and if it is not exactly reduced and fixed long enough by appropriate means,

that is, until bony union occurs, it leads to pseudarthrosis and permanent loss of function.

The rarer type (about 20%) is the abduction fracture, with coxa valga and slight rotation of the leg. The fragments, which are firmly impacted, show a slight angulation with the angle open outwards and in front. It always heals with bony union. If it is held for twelve weeks by means of a short plaster spica in adduction, the head remains normal and the joints mobile.

It was pointed out that from the discussion by Böhler on fracture of the neck of the femur, there were two distinct types with marked differences in prognosis: (i) the adduction type, difficult of treatment and of grave prognosis; (ii) the abduction type, easy of treatment and with a good prognosis for rapid bony union. The method of Cotton was an attempt to convert the adduction into the abduction fracture.

Orbital Abscess.

DR. E. P. BLASHKI demonstrated three cases in which infection had spread from the maxillary antrum and ethmoid labyrinth, leading to the formation of orbital abscess. In the two female patients the spread was subsequent to the performance of intranasal antrum drainage. The boy developed an orbital abscess spontaneously. The condition was accompanied by severe illness, with proptosis and chemosis. The treatment was a radical operation on the ethmoid from the exterior and on the antrum by the Caldwell-Luc method. All these patients developed also an abscess in the orbital fat itself, which presented and was drained through the lower lid. Recovery was quite uneventful.

A Large Mastoid Sequestrum.

Dr. Blashki also showed a man, aged twenty-six years, who was operated on elsewhere two years before coming to the Royal North Shore Hospital and had had a facial paralysis prior to undergoing a radical operation at that time. When seen at the Royal North Shore Hospital six months previously he had had a badly healed left-sided mastoid wound pouring profuse pus; facial paralysis was present on this side. On the right side a chronic suppurative otitis was present. On admission the right ear was submitted to a radical operation and this had progressed to healing in the normal manner.

An attempt was made to clean up the left ear with a view to grafting the facial nerve, but on opening the wound a very large sequestrum was found, consisting of the whole labyrinth and most of the pyramidal portion of the temporal bone. This was removed piecemeal with some difficulty. As there was no hearing apparatus it was thought unnecessary to preserve the external meatus communicating with the cavity. An X ray plate showing the loss of bone was exhibited.

Hyperkinesis.

DR. D. W. H. ARNOTT showed a girl, aged seven years. The patient at birth had been delivered by the breech and was a very delicate and backward baby. Her illness started at the age of nineteen months with an attack of feverishness for one night, which terminated in a sort of convulsion. This was immediately followed by a flaccid right-sided facial paralysis and paresis of the left leg. A few months later she started blinking, and this was soon followed by shrugging of both shoulders. The paralysis of the leg gradually improved and the only indication now was that the left knee jerk was increased and gave a greater response than that of the right knee jerk; there was no weakness present in the leg.

There was still some evidence of right-sided facial palsy, but this had improved greatly in the last year. The abnormal movements, the blinking and the shrugging of the shoulders, had been more or less persistent, but with a gradual improvement of the patient's general condition were becoming less. An attack of whooping cough last year and an attack of measles this year had caused an increase in their activity, and they also increased when she became tired. She was backward intellectually. Emotionally she was very unstable and highly strung and very easily upset. She was restless and fidgety, and a very difficult child to manage. There was no history of rheumatism.

Physically she was well developed. Examination of her nervous system revealed the presence of a right-sided facial paresis, and the left knee jerk was increased and greater than the right. She had a chronic nasal infection with some bronchitis, but this had improved dramatically with cod liver oil emulsion.

Dr. Arnott explained that the patient's abnormal movements would seem to be a direct result of the cerebral disturbance which took place at the age of nineteen months, the nature of which was probably a hæmorrhage. The type of abnormal movement suggested a habit spasm or tic, which was not usually considered of organic origin, but in this case it certainly seemed as if it was. The emotional instability and restlessness would also seem to be a result of the cerebral damage.

Dr. Arnott also showed a boy, aged six years, whose birth had been normal and who developed quite normally until the age of two years and eight months, when he fell on to the back of his head and struck a piece of sharp rock, which made a deep puncture wound of the scalp; ten hours later he became unconscious and was delirious for about an hour.

Three weeks after the accident he started stammering, whereas previous to the accident he had been speaking quite well. A few weeks later abnormal movements commenced. First of all he began screwing his eyes up and blinking, and he developed jerking movements of the limbs. He then began making curious noises and started spitting. After the accident his whole disposition changed; from being a good, even-tempered and easily managed child, he became very restless and fidgety, sleepless, and very difficult to manage. Emotionally he became very unstable and was very easily upset. This state of affairs persisted till a year before the meeting, when Dr. Arnott first saw him at the psychiatric clinic. He was then continuously making grimaces, pulling his face in every direction and spitting; at times he would make silly crowing and grunting noises, and there were jerking movements of the limbs. At this time he was going to school and was so fidgety that he had to be put by himself. His movements also occurred at night when he turned over, but did not occur when he was lying asleep.

Physical examination revealed no abnormality. His symptoms completely disappeared with a rest of three weeks in bed and while taking Fowler's solution. He was free from his symptoms for a period of about eight months, when he was knocked over by a bicycle and received a severe shock, vomiting all night and the next day. Three days later he began to stammer, and the movements and noises returned, and he became sleepless. With this change he became naughty again and fidgety. At the age of five he began to stumble and to fall over, and also became clumsy in his movements and used to drop things out of his hands. This lasted only for a short time.

Dr. Arnott said that it would seem that the head injury was responsible for some cerebral damage and that this damage was responsible for the development of the abnormal movements and also for the complete change in the boy's personality. Here again was what would appear to be a typical case of severe habit spasm originating from cerebral damage, and Dr. Arnott thought that in this and the previous case the abnormal movements were due to some physical change in the neurones.

Dr. Arnott went on to say that the differential diagnosis of the choreas and habit spasms was very difficult and more or less chaotic. He thought that all cases of habit spasms should be treated as chorea till that possibility was definitely excluded. He also thought that the relationship between the two was much closer than was usually considered and that till a clearer understanding was obtained it would be better to include them under the general heading hyperkinesis.

Thrombosis of the Mesenteric Artery.

DR. V. M. COPPLESON showed a male patient, aged eighty-eight years, who had suffered from thrombosis of the mesenteric artery. The patient was admitted to hospital on May 24, 1935, complaining of inability to reduce an inguinal hernia. At the time of admission the patient was vomiting. Examination revealed a large, tense, bluish swelling in the right inguinal region, and also a left indirect inguinal hernia. Operation was performed. A large strangulated hernia, the size of a closed fist, was found. Thrombosis of the mesenteric vessels, supplying four feet of intestine, was present; fluid was found in the hernial sac. A lateral anastomosis was performed and about four feet of bowel were resected between clamps. The inguinal ligament was sutured to the conjoined tendon and the aponeurosis of the external oblique muscle was also sutured. The patient left the theatre in fairly good condition. On his return to the ward he was given 500 cubic centimetres of 5% glucose in saline solution, by the intravenous route. Recovery was uneventful. Dr. Coppleson said that there was some doubt whether the mesenteric thrombosis was the primary condition, or whether it was secondary to the efforts at reduction by taxis prior to the patient's admission to hospital.

Hydatid Cyst of the Lung.

Dr. Coppleson also showed a boy, aged fifteen years, who was admitted to hospital on June 2, 1935, complaining of spitting of blood for two months, matutinal cough for two months, and pain in the left hypochondrium of seven years' duration. The patient lived at Moree, where he was associated with dogs. The history was that the patient spat up blood three years ago. He was treated at a children's hospital, where an X ray examination was made and no sign of hydatid disease in the right lung was found. On the patient's admission to the Royal North Shore Hospital of Sydney an X ray examination was made. A large rounded opacity was seen in each lung. The appearances suggested hydatid cyst. There was some irregularity above the opacity in the left lung, with small cavitation, suggesting abscess of the lung. The Casoni test, owing apparently to faulty fluid, gave no reaction. Of the leucocytes, 7% were eosinophile cells. The hydatid cyst in the right side of the lung was removed by a two-stage operation. Dr. Coppleson said that the interest of the case lay in the fact that an X ray examination carried out three years previously showed that the right lung was clear. The large hydatid cyst which had been removed must therefore have grown to the size shown in the skiagram within three years.

Correspondence.

THE AUTONOMIC NERVOUS SYSTEM.

SIR: Professor Burkitt has kindly forwarded to me a copy of the papers by Dr. Phillips and himself, and I request the favour of making a few remarks in reply.

First I would like to thank the authors for their generous expression of appreciation of my humble effort and of the difficulties associated with the presentation of a subject like the one in question in the short space of an hour or two. Many important and fundamental facts must be omitted and others only briefly referred to, until one almost gives up in despair of ever presenting adequately, concisely and simply the main facts which can provide a skeleton for further reading and awaken a desire in the minds of the audience to go and delve more deeply into the subject for themselves. Also diagrams which are drawn in the interest of simplicity, unless fully explained, can, it is apparent, be misinterpreted. This applies to Figure I, which is criticized by Dr. Phillips. When I drew this sketch, the line marked "S" was at first connected with all the sensory endings shown, as well as with the centres indicated in the cord, and this is how it is still shown in my lantern slide. Just before sending my original sketch to the publishers, however, I altered it so that the various endings were shown separately, in case there should be any misunderstanding. Unfortunately the line from the sensory ending on the blood vessel was missed and appears as originally drawn, and certainly does tend to convey the impression which Dr. Phillips mentions. The line "S", however, is meant to represent the ultimate connexions of sensory endings in general, and not any one sensory neurone in particular. It is intended to indicate that impulses arising in various types of sensory endings pass via the afferent pathway "S" into the cord, where they can ultimately reach the motor centres of the autonomic and the somatic systems. This was made quite clear at the time, but in writing up my lecture for publication this explanation of the diagram, which would have made its meaning quite clear, was overlooked. The same applies to the lines labelled "Desc." This merely indicates that impulses flowing from higher centres, during voluntary activity influence the lower centres. No actual neurones are meant to be indicated or implied. If all the lines which would be required to give an absolutely complete and accurate indication of all neurones involved in this mechanism had been put in the diagram, it would have been so crowded as to be useless.

With regard to Dr. Phillips's statement concerning the mode of termination of pyramidal fibres, I may state that I am quite familiar with the work of Hoff and Hoff on the degeneration of the "*boutons terminaux*", and therefore can agree with him in the main. Dr. Phillips will pardon me, however, if I state that he now has laid himself open to the charge of inaccuracy, as he states that the Hoffs have shown that no pyramidal fibres end in relation with the cells of the anterior horn, but all end around cells at the base of the posterior horn. While this is the rule, the Hoffs, in giving the results of experimental degeneration of pyramidal fibres, definitely state that while "the predominant area of degeneration (that is, of the terminal buttons) is in the intermediate zone, the whole ventral horn is 'peppered' with degenerated *boutons*. This is even more obviously the case in the chimpanzee, where *bouton* degeneration was found on cells in the ventral horn, including motor neurons." (*Brain*, Part IV, 1934, page 472, second paragraph.) It is quite evident then that some of the pyramidal fibres do terminate in relation with the motor cells of the anterior horn.

Taking *seriatim* the other points raised. I fully agree with the remarks made by Professor Burkitt concerning the centres postulated by physiologists and referred to as "cardio-accelerator" *et cetera*. At the time I made it quite clear that no group of cells in the floor of the fourth ventricle could be definitely identified in sections of the brain stem as the nuclei concerned, but that I believed that the centres were anatomical entities and would probably be represented by cells somewhere in the region of the dorsal nucleus of the vagus.

With regard to the diencephalon, I deliberately chose as most instructive and important the brilliant work of Le Gros Clark, who has traced the phylogenetic development of the diencephalon throughout the vertebrates. I quite agree with Professor Burkitt that a proper conception of the diencephalon can be obtained only by a comparative study of the complete vertebrate series, and this is how it is presented to my neurological students, but to do this adequately requires several lectures and so it was not possible for me to do more than summarize the essential facts arrived at by Le Gros Clark, and then only so far as human brain anatomy is concerned. With regard to the question of nomenclature, I personally prefer Le Gros Clark's as being fundamental and as being arrived at by just that comparative study which Professor Burkitt says is so essential to the complete understanding of the region. Nevertheless the description given by Professor Burkitt is well known and is a very useful addition to the description given of the hypothalamus.

Dr. Phillips's contribution concerning the fundamental difference in the activity of somatic and autonomic systems *et sequentes* is very valuable, but can hardly be given in correction of the impression conveyed by the words of my

paper which he criticizes, namely, that "there can be no action of the somatic system without coincident action of the autonomic system". It does not seem to me to be fair to assume, as Dr. Phillips does, that I implied that the reverse of this is the case. In my lecture I was emphasizing the relation of the two systems and was referring especially to voluntary activity. I still think I am not far wrong in stating that every voluntary effort is accompanied by activity in the autonomic system. I agree with Dr. Phillips, however, that as a rule it is dangerous in the interests of absolute accuracy to make sweeping statements, but I do not think that, in the circumstances, the truth has here been in any way distorted.

Concerning the paragraph on "Chemical Factors", I am very much indebted to Dr. Phillips for his lucid summary. I must confess that as no copy of Ballance's work is available in Adelaide, I was fully dependent on an abstract in *Nature* (January, 1935, page 73) for the information given. For the purpose of the lecture, however, no harm is done if the word "cortex" at the end of the first paragraph is altered to "central nervous system", which was rather the idea I wished to convey, although, of course, if I wished to quibble, there is no reason for disbelieving the possibility of the muscle again coming, in time, under the influence of the cortex.

Concerning other points raised and considered by the authors as worthy of mention, it is, after all, only a matter of the difficulty mentioned above—of deciding what to put in and what to leave out. As Professor Burkitt says, no summary of a subject is completely satisfying to everyone. Almost every section can readily be made the subject of a lecture, or series of lectures, and even then the matter presented would depend entirely upon personal choice.

In conclusion, I must thank Professor Burkitt and Dr. Phillips for taking the trouble of pointing out what appeared to them to be inaccuracies in the paper. Needless to say, we all strive to be as accurate as possible in all circumstances, but it is quite easy for us teachers to regard as obvious what might be misleading to others. I quite agree with Dr. Phillips that "in research, rule is the substance and exception the sauce", but these remarks are hardly applicable in reference to a lecture which is not prepared for experts, but only pretends to be a summary of selected essentials. As a teacher, I fear that too much detail not only tends to dry up interest and to confuse one's audience, but makes the grasp of fundamentals more difficult.

Yours, etc.,

H. J. WILKINSON.

Adelaide,
South Australia,
September 18, 1935.

AN INTERMEDIATE OPHTHALMIC SERVICE.

SIR: The letter written by Dr. E. L. Gault on the above subject in your issue of November 9 deserves the earnest attention of all oculists and represents the views of a considerable number of Melbourne specialists.

In my opinion the New South Wales scheme fails mainly in two cardinal features. In the first place it makes no provision for patients to consult their chosen oculist at his private consulting room. This to me seems a fundamental defect and is totally opposed to the British idea of such a service, the report upon which, in page after page, stresses the fact that the relationship between the specialist and the patient should approach as nearly as possible that obtaining in ordinary private practice. How can any institutional treatment fulfil such a condition? In the second place, the fee (10s.) paid to the oculist bears no reasonable relation to the time and skill which must be given refraction and eye examination and a prescription for glasses. It would seem practically inevitable that the work must be hastily and poorly done, quite unworthy of the profession and equally unsatisfactory to the public. The fee agreed upon under the British scheme (10s.—the same as in Sydney), which can be met by those living in overcrowded industrial communities in Britain, cannot surely apply to people working under normal Australian conditions.

It can be safely asserted that the majority of the public interested in any intermediate service would unquestionably prefer a consultation at the private rooms of the oculist of their choice rather than at any institution, and would be prepared to pay a reasonably adequate fee for such a privilege. Again, we are credibly informed that there is a great difference of opinion among the oculists of Sydney about the intermediate service now on trial there, practically half of them being in its favour and the other half as definitely against it. Something very similar has occurred in Melbourne, and as in this city there are definite conditions, such as oculists attached to lodges and other things which do not obtain in Sydney, the treatment of such patients in an institution would have even less to recommend it than in other States.

Since ultimately an intermediate service of some sort will probably form part of a general scheme of national insurance, in which all specialists will be included, it seems to me supremely important to examine very carefully all the conditions of any such proposed service and to take a very long view, for all history teaches us that the remote results of movements, which seemed to offer many blessings when initiated, often have been vastly different from anything which might reasonably have been expected. We must look well before we leap.

Yours, etc.,

ERNEST R. SAWREY.

Masonic Chambers,
31, Collins Street,
Melbourne, C.1,
November 16, 1935.

A CASE OF POLYCYTHÆMIA BECOMING A LYMPHATIC LEUCHÆMIA.

SIR: A patient was diagnosed ten years ago as suffering from *polycythæmia vera*. He was under medical supervision and treatment for about six years. During this time and up to the last blood examination in 1930 his red cell count varied from eleven millions to seven millions per cubic millimetre. In 1930 the red cells numbered 10,210,000 and the white cells 20,100 per cubic millimetre.

Recently the patient became concerned about his general condition and a blood examination revealed:

Red cells, per cubic millimetre	2,818,000
Hæmoglobin value	62%
Colour index	1·0
White cells, per cubic millimetre	65,400
Polymorphonuclear cells	18%
Lymphocytes	82%

Cases are on record in which a polycythæmia became a myeloid leuchæmia, but I cannot discover any reference to a lymphatic leuchæmia. Can any of your readers quote a case or reference thereto?

Yours, etc.,

A. E. FINCKH.

227, Macquarie Street,
Sydney,
October 28, 1935.

TREATMENT BY OLIVE OIL EMULSION.

SIR: As Dr. V. G. Walsh, one of the world's leading physiologists, and the man responsible for a large volume of important original work in medicine, physiology, and physical chemistry, saw fit to entrust to me the pioneering of this method of treatment in Sydney, it becomes my obvious duty to reply, as adequately as lies in my power, to the amazingly uninformed letter of Professor Davies in THE MEDICAL JOURNAL OF AUSTRALIA of November 23.

The issues raised must be dealt with *seriatim*. Professor Davies deplores the "lack of adequate data to support the claims made on behalf of olive oil emulsion". There is no

lack of such data, and the only conclusion one can reach is that the professor fails to read the journal devoted to his own special subject. May I refer him to the *Journal of Physiology*, Volume LXXVIII, 1933, Number 4, page 467 (Walsh, V. G., and Frazer, A. C.).

Still on the subject of "lack of adequate data", will the professor please read in *The British Medical Journal* of March 10, 1934, a paper entitled "The Effects of Subcutaneous and Intravenous Injections of Toxins Combined with Fine Emulsions of Oils", by V. G. Walsh and A. C. Frazer (from the Department of Physiology, Saint Mary's Hospital Medical School).

In *The British Medical Journal* of March 17, 1934, page 504, Dr. G. Norman Myers, of the Pharmacological Laboratories, Cambridge, confirms the work of Walsh and Frazer, although he is wrong in claiming priority as to the date of his own experiments. The work of Walsh and Frazer was completed in 1930. This has been confirmed by Professor Collingwood in *The British Medical Journal*, March 24, 1934, page 557.

I agree with Professor Davies that a purely medical subject should not be exploited by the lay Press. No publicity has been sought, but some has been acquired from various hospitals and people using the emulsion by the newspapers concerned. As a result of this publicity supplies of the emulsion have been sought and many lives have been saved in consequence. Is this not important enough to make other consideration appear very small?

All my cases were treated in collaboration with the regular medical attendants, whether in hospitals or in private practice. In each instance I particularly requested the doctor concerned to report his case or cases, and I refrained from doing so to allow time for such case reports to be published.

As regards the "scathing editorial comment" in *The British Medical Journal* of March 30, 1935, if the professor will read that annotation again, he will find the editor merely registered a complaint that Dr. Walsh delivered a lecture before a conference of eminent physical chemists, held at University College, under the chairmanship of Professor Donnan, F.R.S., instead of addressing a medical gathering. Professor Davies should take the trouble to read the reply of Dr. A. C. Frazer, published in *The British Medical Journal* of April 6, 1935. If he, in his search for truth, will obtain also a copy of the volume in which the paper mentioned appeared, he will see a statement in Professor Donnan's foreword to the effect that this discovery presages a new era in the history of medicine. In this volume, entitled "Technical Aspects of Emulsions", the machine used to make this preparation is described, and a case of pneumonia is cited.

Professor Davies is surely not serious when he writes: "The adsorption of toxins may be a plausible hypothesis, but lacks adequate proof." In this statement he relegates to the scrap-heap the work of many eminent physiologists and physical chemists, including Collingwood, Walsh and Frazer of Saint Mary's, Myers of Cambridge, Donnan and Potts, and of the workers in Donnan's laboratory (Lewis, Ellis, Powis, and Barker), who amplified and extended the surface tension theory of emulsions and correlated it with adsorption and electrical charges. The professor is mistaken again when he asserts: "One finds very little reason to believe that toxins, actual or hypothetical, are selectively adsorbed by an emulsion of olive oil." In answer to this I would refer him again to the papers cited above, wherein adequate proof of this phenomenon is given. I have repeated the animal experiments personally, and so confirmed the work of Walsh and Frazer before I injected the emulsion into my own veins and later into patients.

Professor Davies, in his consideration of a second aspect "from the scientific point of view", is floundering in a morass of uncertainty. Walsh proved (published in the *Journal of Physiology* again) that the rate of adsorption of fats from the intestine depends directly on the size of the dispersed phase of the emulsion presented to the intestinal villi. The fats (either directly or after separation of their glycerine) are emulsified by the alkaline pancreatic juice, aided by the presence of such protective colloids as mucin, cholesterin, and the like. The statement of so-called facts regarding the physiology of fat adsorption from the intestine is entirely erroneous, considered in the light of modern research. Emulsions of liquid paraffin made with the same machine show the same adsorption phenomenon. The professor refers to the chyle passing up the thoracic duct as a "fine emulsion". If he takes the trouble to compare microscopically this chyle with the olive oil emulsion it might begin to dawn on him just why the chylous emulsion in the blood stream is inadequate to adsorb any appreciable quantity of toxin. At present a dispersion of the oil is being attained in which the largest globules average 0·2 micron. During the experimental work of Walsh and Frazer, cod liver oil, arachis oil, olive oil and liquid paraffin were used successfully. In *The British Medical Journal* of March 10, 1934, these workers publish a case report wherein a finely emulsified cod liver oil was intravenously injected.

Now, in view of the foregoing, and assuming the professor will consult the references cited above, is it really necessary to reply to the concluding paragraph of his letter? Were it possible to collect 500 or 1,000 women in the throes of puerperal septicæmia within, say, thirty-six hours of the onset, and one were allowed to inject intravenously twenty cubic centimetres of 5% olive oil emulsion every three hours until each patient had received sixty cubic centimetres, one could guarantee an equal number of well women in twelve hours. Professor Davies claims the oil by mouth is just as efficient. He would be bound then to give each patient a three-hourly dose of one cubic centimetre of olive oil by mouth, and, according to him, he also should be able to guarantee the cure of his patients. Would all the psychological effects in the universe aid him?

In conclusion, I would again ask every medical man who has so kindly collaborated with me in this work to refute in print the absurd contentions of the Professor of Physiology.

I am sending copies of Professor Davies's letter overseas to Dr. Walsh, to Professor Donnan, to Dr. G. Norman Myers, of Cambridge, and I am sure they will reply more adequately.

Yours, etc.,

A. J. FITZGERALD.

"Craignish",
185, Macquarie Street,
Sydney,
November 24, 1935.

AN APPEAL.

SIR: The Council of the Medical Benevolent Association of New South Wales is appealing to the members of the medical profession in New South Wales for contributions to a fund for furnishing Christmas comforts and cheer to the unfortunate members of the profession and their dependants.

Any surplus after the allocation of an adequate sum to each beneficiary will be placed to the credit of the general fund of the Association.

All contributions should be sent to Dr. E. S. Littlejohn, Honorary Treasurer, 135, Macquarie Street, Sydney.

Yours, etc.,

J. M. GILL,
Honorary Secretary.

135, Macquarie Street,
Sydney,
November 21, 1935.

Obituary.

HUBERT CECIL CONDELL CARDEN.

WE regret to announce the death of Dr. Hubert Cecil Condell Carden, which occurred on November 15, 1935, at Adelaide, South Australia.

The Royal Australasian College of Surgeons.

MEETING OF THE BOARD OF CENSORS.

THE next meeting of the Board of Censors of the Royal Australasian College of Surgeons will be held in Sydney in March, 1936.

Candidates who desire to present themselves at this meeting should apply to the Censor-in-Chief for permission to do so on or before December 31, 1935. The appropriate forms are available at the College, Spring Street, Melbourne, and at the offices of the various State secretaries.

Proceedings of the Australian Medical Boards.

QUEENSLAND.

THE undermentioned has been registered, pursuant to *The Medical Acts*, 1925 *to* 1933, of Queensland, as a duly qualified medical practitioner:

Webster: Charles Ivo William, M.B., B.S., 1934 (Univ. Melbourne), Nambour.

Books Received.

SPANISH INFLUENCE ON THE PROGRESS OF MEDICAL SCIENCE, WITH AN ACCOUNT OF THE WELLCOME RESEARCH INSTITUTION AND THE AFFILIATED RESEARCH LABORATORIES AND MUSEUMS FOUNDED BY SIR HENRY WELLCOME, LL.D., D.Sc., F.R.S.; Commemorating the Tenth International Congress of the History of Medicine held at Madrid; 1935. London: The Wellcome Foundation, Limited. Medium 8vo., pp. 121, with illustrations.

PROGNOSIS, Volume I, published by The Lancet Limited; 1935. Demy 8vo., pp. 384. Price: 10s. 6d. net.

A GUIDE TO HUMAN PARASITOLOGY FOR MEDICAL PRACTITIONERS, by D. B. Blacklock, M.D., D.P.H., D.T.M., and T. Southwell, D.Sc., Ph.D., A.R.C.Sc., F.Z.S., F.R.S.E.; Second Edition; 1935. London: H. K. Lewis and Company, Limited. Royal 8vo., pp. 268, with illustrations. Price: 12s. 6d. net.

Diary for the Month.

DEC. 10.—Tasmanian Branch, B.M.A.: Branch.
DEC. 10.—New South Wales Branch, B.M.A.: Ethics Committee.
DEC. 12.—New South Wales Branch, B.M.A.: Branch.
DEC. 13.—Queensland Branch, B.M.A.: Annual Meeting.
DEC. 17.—Tasmanian Branch, B.M.A.: Council.
DEC. 17.—New South Wales Branch, B.M.A.: Medical Politics Committee.
DEC. 20.—Queensland Branch, B.M.A.: Council.

Medical Appointments Vacant, etc.

FOR announcements of medical appointments vacant, assistants, *locum tenentes* sought, etc., see "Advertiser", pages xx, xxi, xxii.

HEATHERTON SANATORIUM, CHELTENHAM, VICTORIA: Resident Medical Officer.

ST. GEORGE DISTRICT HOSPITAL, KOGARAH, NEW SOUTH WALES: Senior Resident Medical Officer.

THE BRISBANE AND SOUTH COAST HOSPITALS BOARD, QUEENSLAND: Honorary Physician.

Medical Appointments: Important Notice.

MEDICAL practitioners are requested not to apply for any appointment referred to in the following table without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

BRANCH.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 135, Macquarie Street, Sydney.	Australian Natives' Association. Ashfield and District United Friendly Societies' Dispensary. Balmain United Friendly Societies' Dispensary. Friendly Society Lodges at Casino. Leichhardt and Petersham United Friendly Societies' Dispensary. Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney. North Sydney Friendly Societies' Dispensary Limited. People's Prudential Assurance Company Limited. Phœnix Mutual Provident Society.
VICTORIAN: Honorary Secretary, Medical Society Hall, East Melbourne.	All Institutes or Medical Dispensaries. Australian Prudential Association, Proprietary, Limited. Mutual National Provident Club. National Provident Association. Hospital or other appointments outside Victoria.
QUEENSLAND: Honorary Secretary, B.M.A. Building, Adelaide Street, Brisbane.	Brisbane Associate Friendly Societies' Medical Institute. Chilliagoe Hospital. Members accepting LODGE appointment and those desiring to accept appointments to any COUNTRY HOSPITAL, are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.
SOUTH AUSTRALIAN: Secretary, 207, North Terrace, Adelaide.	All Lodge appointments in South Australia. All Contract Practice Appointments in South Australia.
WESTERN AUSTRALIAN: Honorary Secretary, 205, Saint George's Terrace, Perth.	All Contract Practice Appointments in Western Australia.
NEW ZEALAND (Wellington Division): Honorary Secretary, Wellington.	Friendly Society Lodges, Wellington, New Zealand.

Editorial Notices.

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